

CAPACITACIÓN INTRODUCCIÓN A LA VIGILANCIA GENÓMICA EN EL MARCO DE LA PANDEMIA COVID-19

- Introducción al genoma del SARS-CoV-2.
Mutaciones de interés biológico. Variantes de interés y variantes de preocupación. Conceptos generales y variantes circulantes en Argentina.

10 de Septiembre de 2021

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Lab. Nac .Referencia Sarampión y Rubéola, OPS/OMS y Min Sal

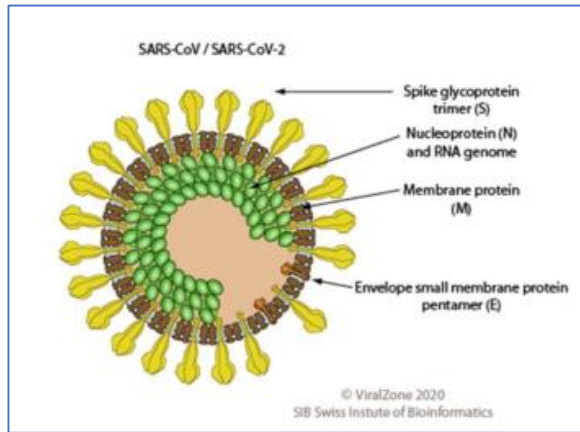
INEI-ANLIS "Dr. Carlos G. Malbrán"

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Directora Maestría Microbiología Molecular UNSAN-ANLIS



CARACTERÍSTICAS DE LOS VIRIONES DE SARS-CoV-2

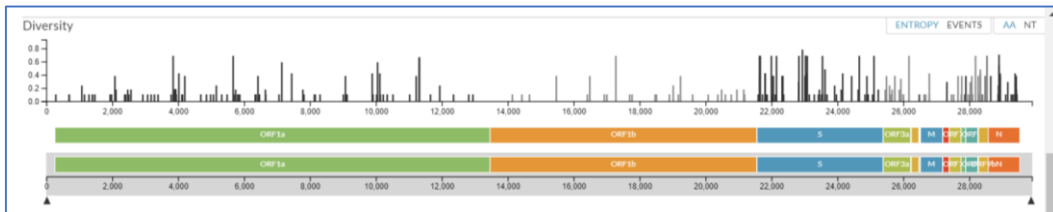
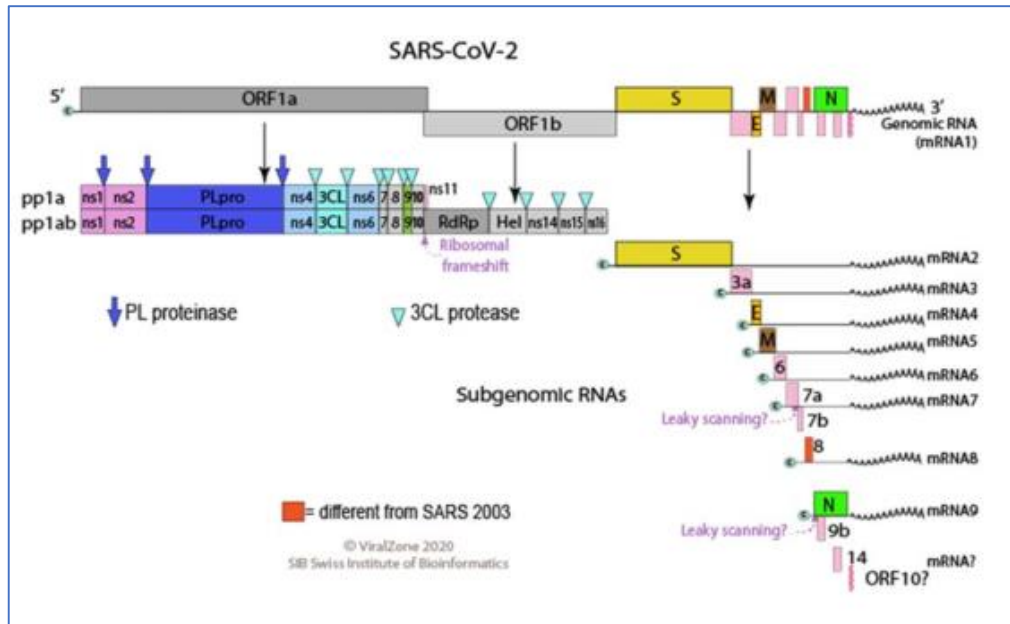


Familia: **Coronaviridae**, **Orden Nidovirales** **Subfamilias** Torovirinae y **Coronavirinae**. Los **Subfamilia** Coronavirinae, **Géneros:** Alpha-, **Beta-**, y Gammacoronavirus. Alfa- y betacoronavirus tienen hospedadores **mamíferos**. Gammacoronavirus infectan aves.

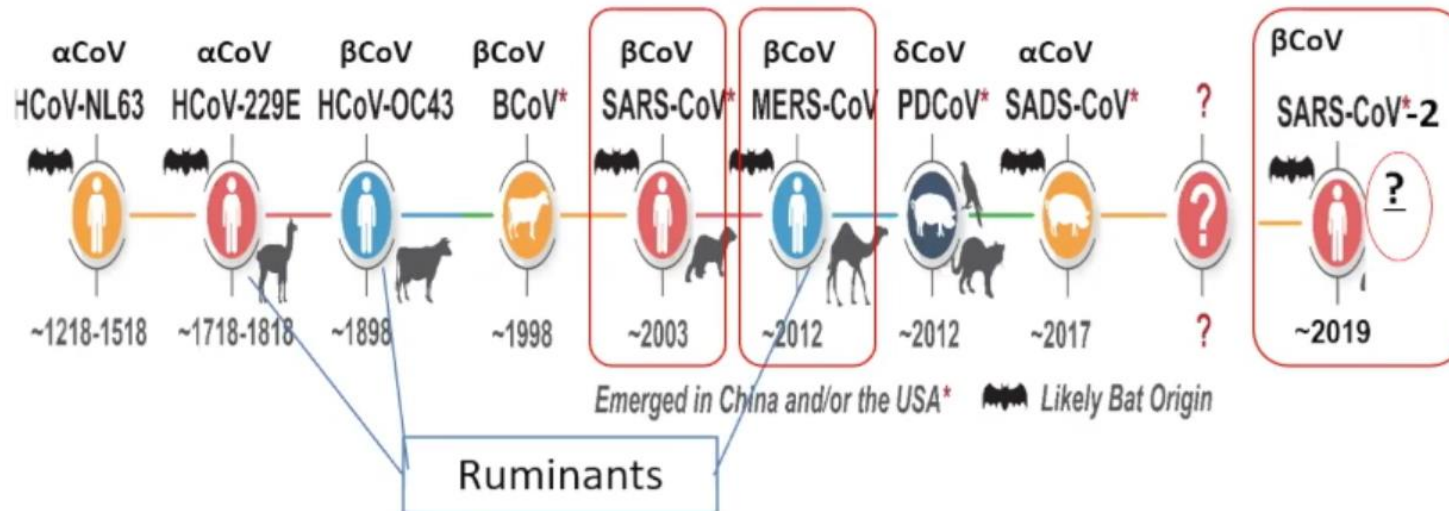
Partículas esféricas, con rango de tamaño de 50 a 200 nm y un diámetro promedio de 118-136 nm. Las proteínas S, E y M se insertan en envoltura. Nucleocápside estructura helicoidal. Genoma RNA de simple cadena de polaridad positiva, de 26-32 kb.

Se traducen 27 proteínas, 16 proteínas no estructurales y 4 proteínas estructurales, necesarias para cumplir el ciclo de replicación completo.

Proteínas estructurales: S, N, E, M,
Proteínas no estructurales: NSP 1-16
Proteína no estructurales “accesorias” como HE, 3a/b y 4a/b



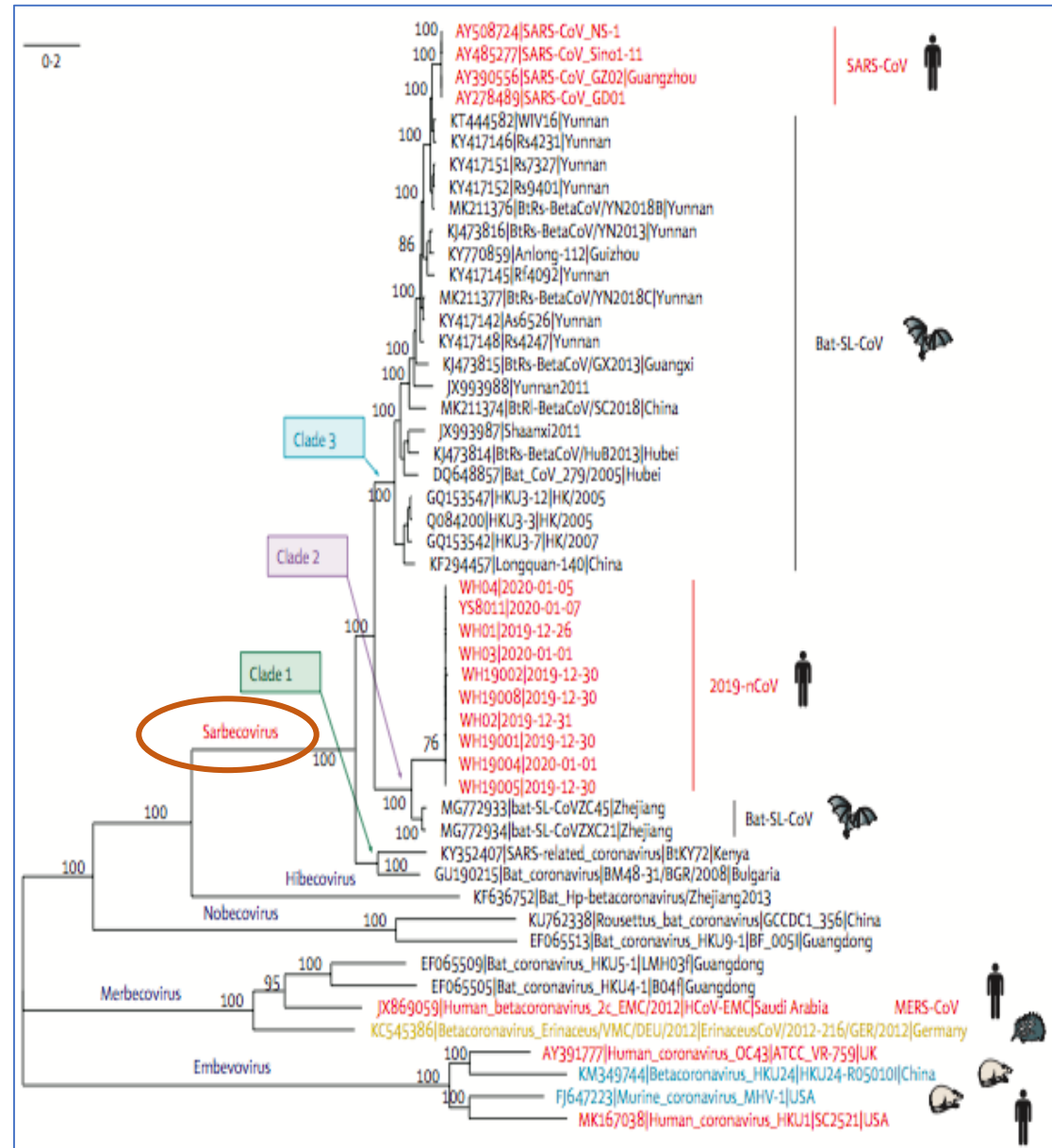
Spillover and Emergence of new CoVs occurs repeatedly in humans and livestock

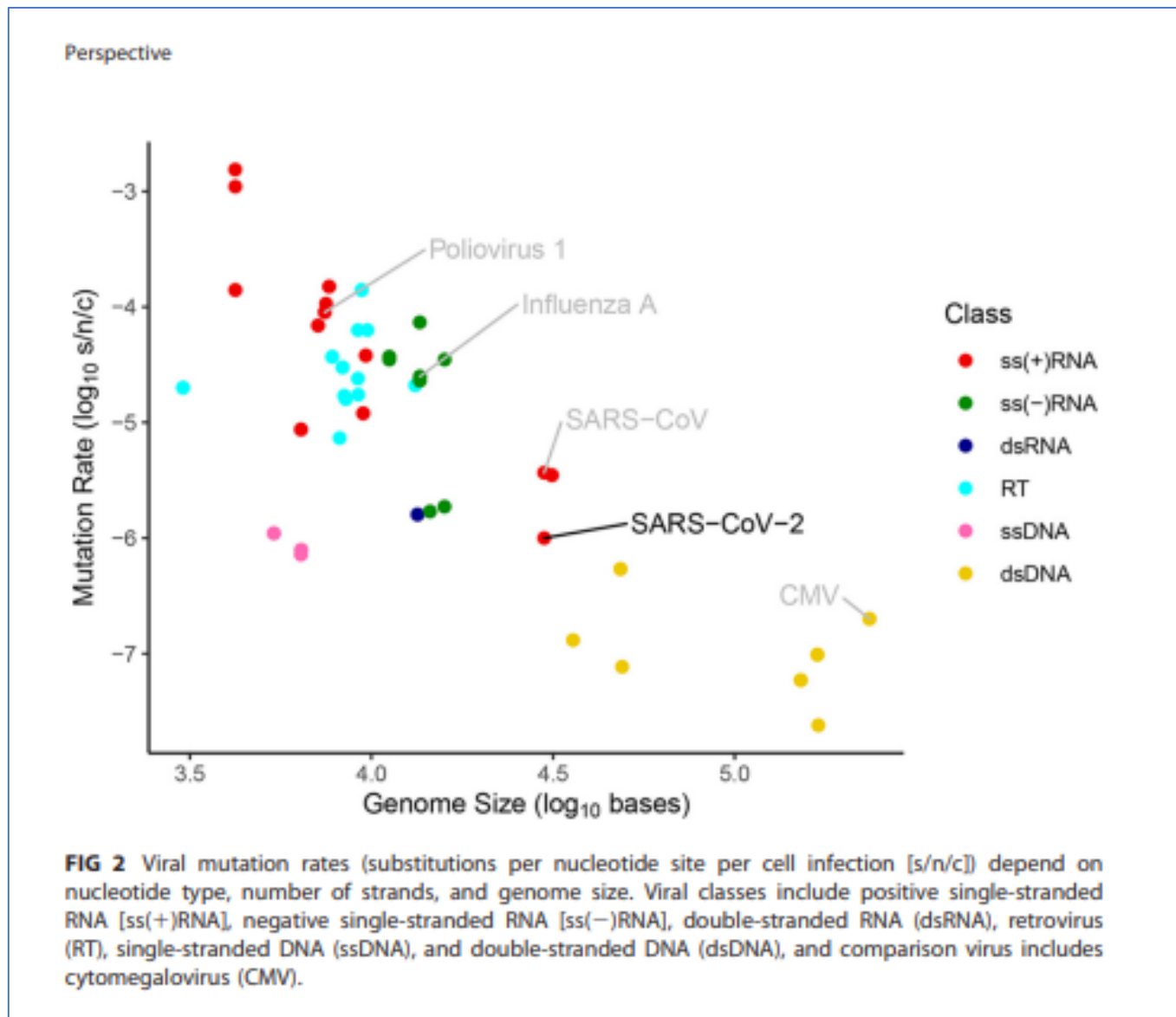


(Modified, Courtesy of P. Daszak, 2018)

SARS CoV was not the first CoV transmitted from animals to humans;
CoVs associated with the common cold are endemic in humans

Phylogenetic analyses of nCoV





Temporal Dynamics and Evolution of SARS-CoV-2 Demonstrate the Necessity of Ongoing Viral Genome Sequencing in Ontario, Canada Calvin P. Sjaarda, a,b Jennifer L. Guthrie, c Samira Mubareka, d,e Jared T. Simpson, f,g Bettina Hamelin, h Henry Wong, i Leanne Mortimer, j,k,l Robert Slinger, l,m Andrew G. McArthur, n,o,p Marc Desjardins, j,q Allison McGeer, r,s Tony Mazzulli, c,e,r Katya Douchant, t Danielle Brabant-Kirwan, u Ramzi Fattouh, v Aaron Campigotto, e,w Samir N. Patel, c,e Nahuel Fittipaldi, c,e,s Robert I. Colautti, x Prameet M. Shethi,t,y,z for the Ontario's COVID-19 Genomics Rapid Response Coalitio MsPHERE. May 5;6 (3):3 e00011-21

SARS-CoV-2 Genetic Characterization

General considerations:

- Mutations are expected natural events in the evolution of viruses and in their adaptation process.
- Usually, this type of virus (RNA) is more prone to generate mutations and, therefore, to generate genetic variations.
- There are different types of mutations, some more important than others

Genetic groups, Lineages, Variants...



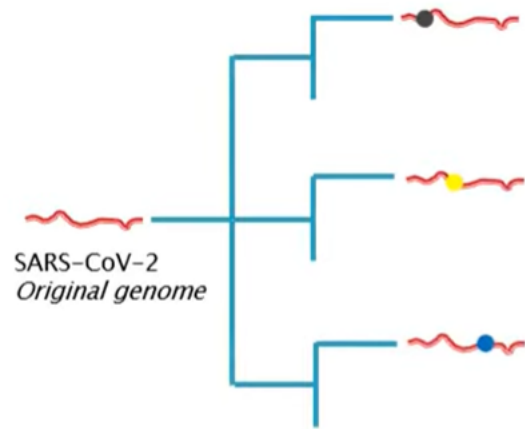
SARS-CoV-2
Original genome



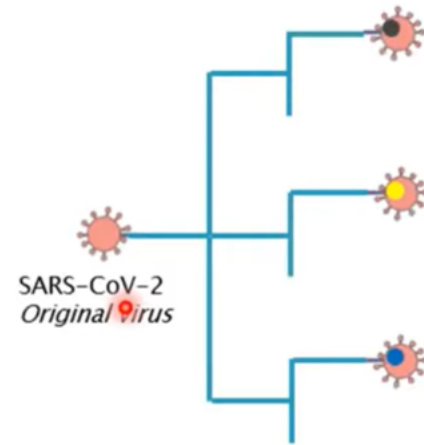
SARS-CoV-2
Original virus



Genetic groups, Lineages, Variants...

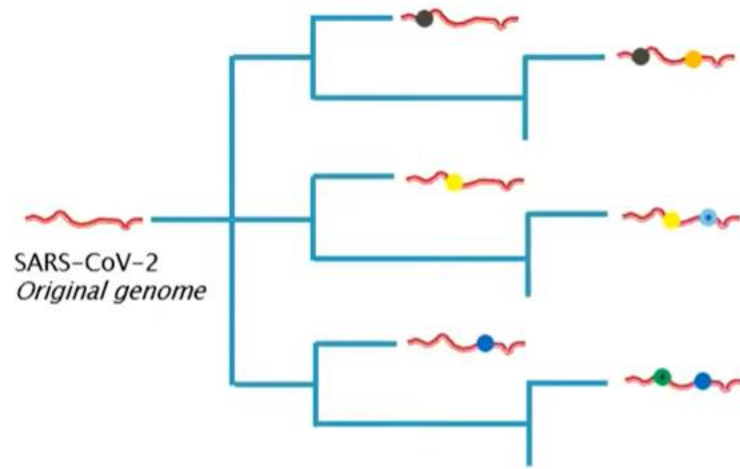


Genetic group



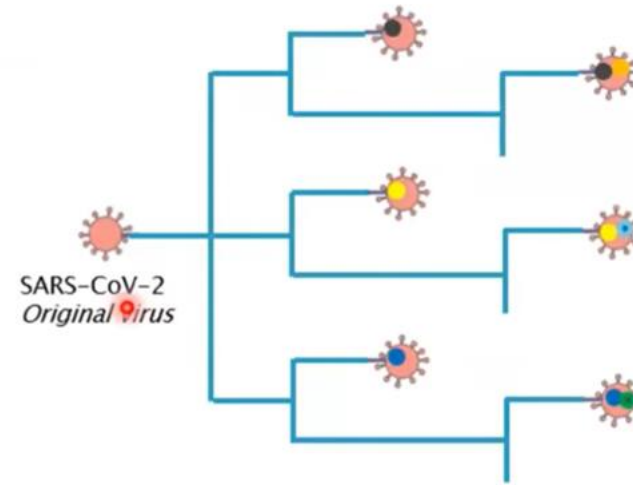
Genetic group

Genetic groups, Lineages, Variants...



Genetic group

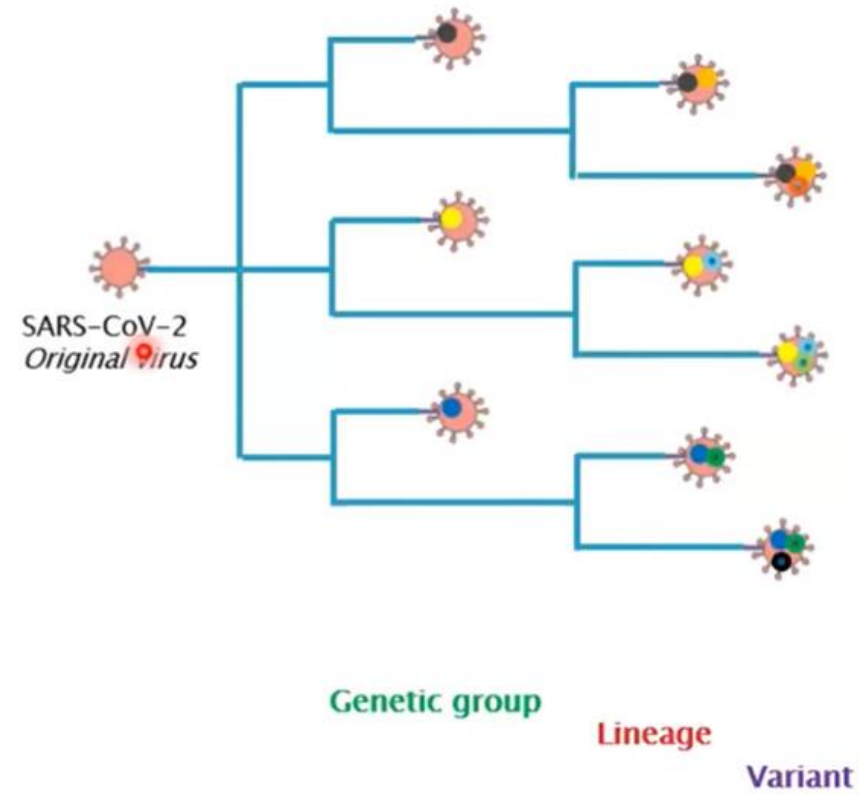
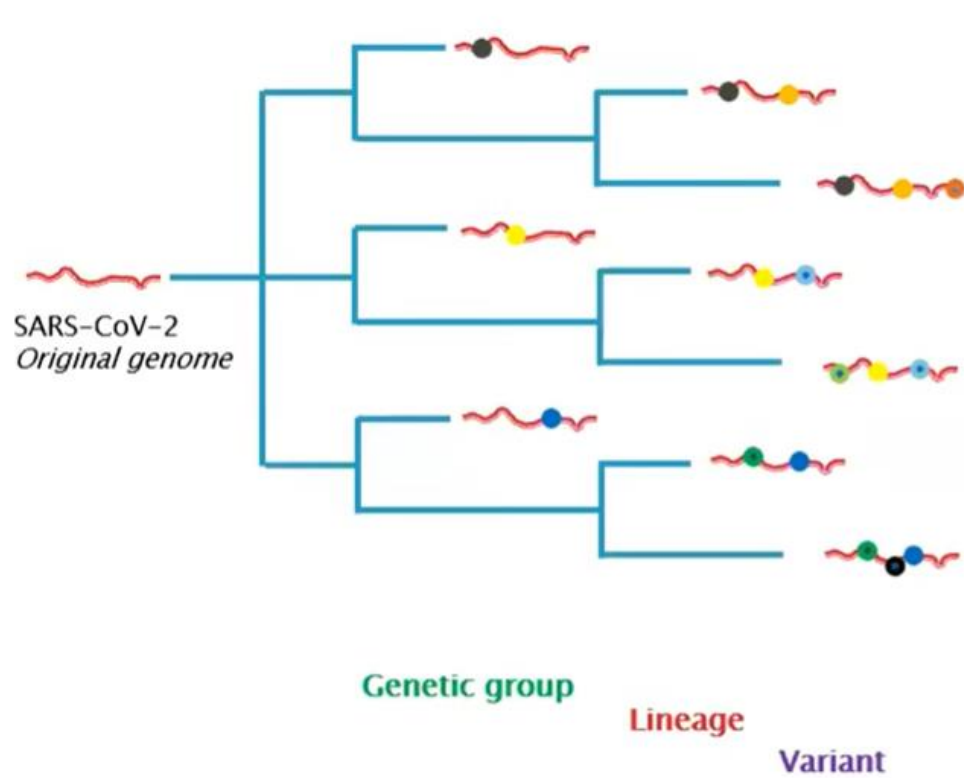
Lineage



Genetic group

Lineage

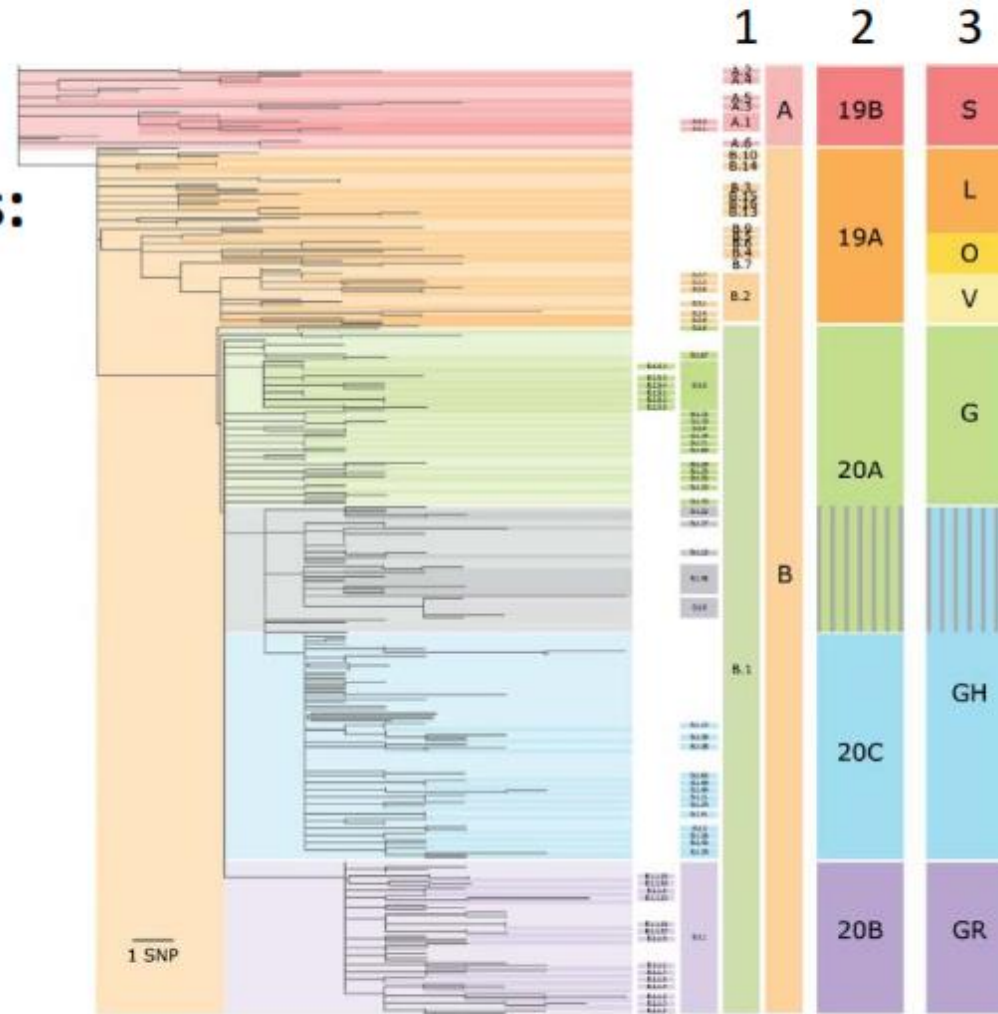
Genetic groups, Lineages, Variants...



SARS-CoV-2 clades:

Clade naming conventions:

1. Pangolin Lineages
 - cov-lineages.org
2. Clades by Nextstrain *****
 - nextstrain.org
3. Clades by GISAID
 - gisaid.org



Adapted from [Alm et al. 2020](#)

Rationale for sequencing of SARS-CoV-2

- Monitor trends at the national level
 - Monitor emergence of important new strains
 - Monitor trends after interventions such as vaccination
- Better understand epidemiology at the local level
 - Investigate transmission in healthcare settings
 - Investigate clusters in other settings
 - Reveal important, unsuspected clusters
 - Provide evidence for or against suspected transmission

SARS-CoV-2 Genetic Characterization

General considerations:

- **What is a mutation? Is a biological / chemical (frequent) change that occurs in the genetic material**

AGTTGAGTAGTTGAATGTATGA

AGTTGGTAGTTGAATATATGA

GGTTGGTAATTGAATATATAA

AGTGGGGTAGTTGAATATATGG

Some mutations are detrimental to the virus

Some mutations (most of them) are neutral

Some mutations are advantageous for the virus

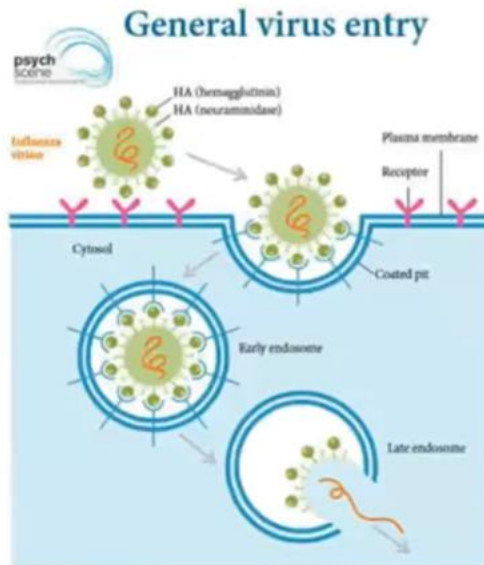
SARS-CoV-2 Genetic Characterization

Why does the virus change? What are the possible consequences?

- The changes can bring advantages to the virus to *achieve* its objectives:
 - To improve the ability to enter cells and then replicate
 - To escape the immune response (natural or by vaccine)

SARS-CoV-2 Genetic Characterization

- To improve the ability to enter cells and then replicate



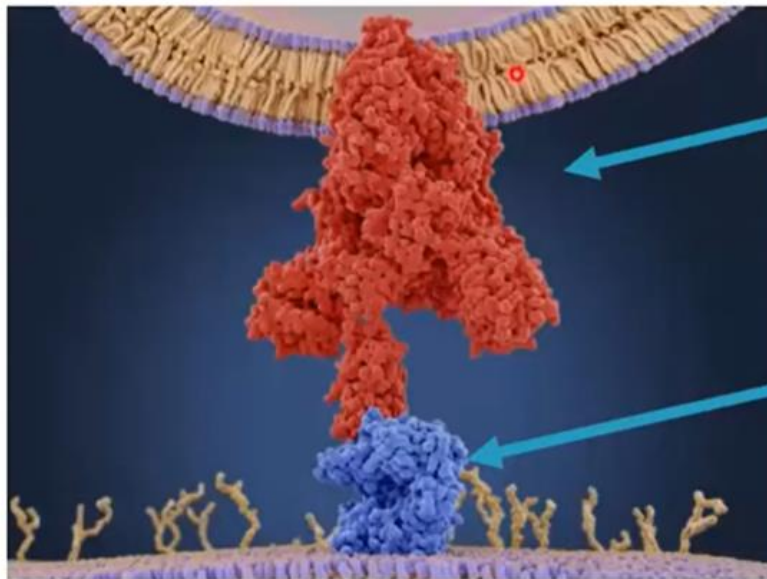
Viruses need to enter a cell to replicate

Killing their host is not convenient!

<https://psychscenehub.com/psychinsights/covid-19-and-the-brain-pathogenesis-and-neuropsychiatric-manifestations-of-sars-cov-2-cns-involvement/>

SARS-CoV-2 Genetic Characterization

- To improve the ability to enter cells and then replicate



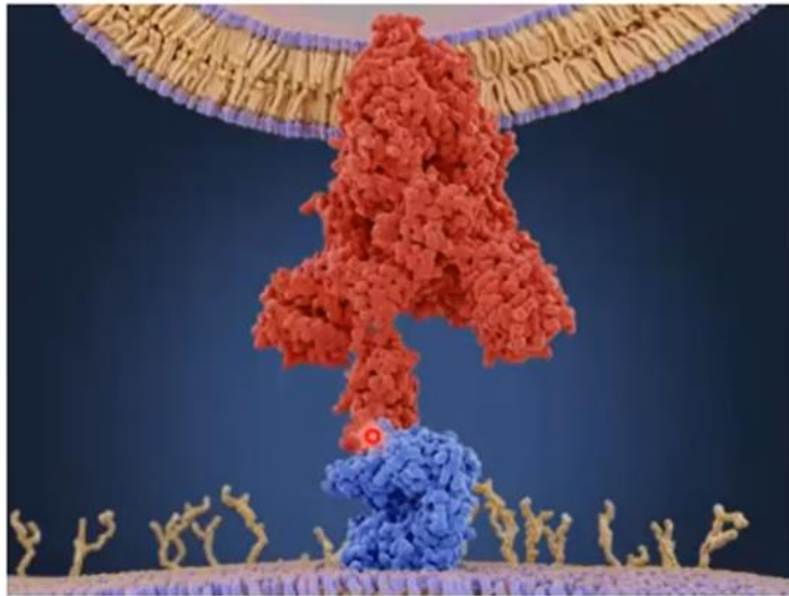
Spike protein

Angiotensin-Converting Enzyme Receptor (ACE)

<https://www.clinicalomics.com/topics/patient-care/coronavirus/research-may-explain-why-men-are-more-susceptible-to-covid-19-than-women/>

SARS-CoV-2 Genetic Characterization

- To improve the ability to enter cells and then replicate



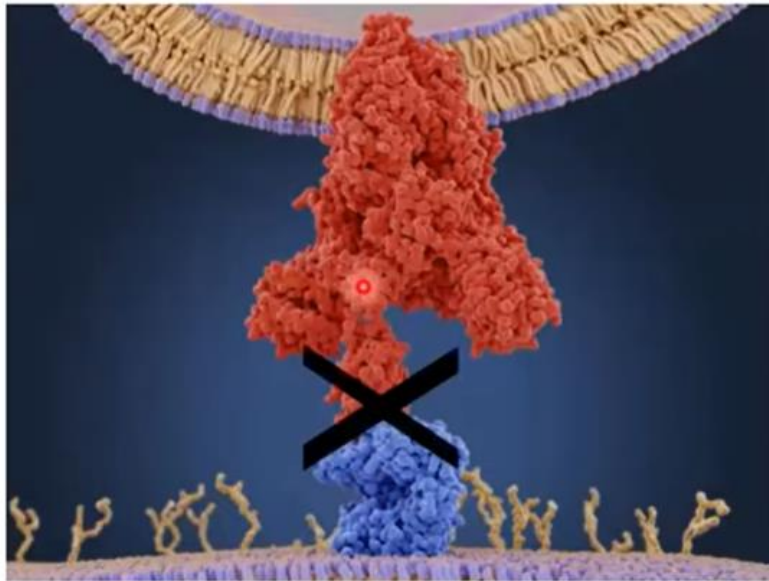
<https://www.clinicalomics.com/topics/patient-care/coronavirus/research-may-explain-why-men-are-more-susceptible-to-covid-19-than-women/>

Genetic Group		Reference mutations for the genetic group	Mutations on the S protein
S	A	C8782T, T28144C, NS8-L84S	
L	B	C241, C3037, A23403, C8782, G11083, G25563, G26144, T28144, G28882	
V	B.2	G11083T, G26144T, NSP6-L37F, NS3-G251V	
G	B.1	C241T, C3037T, A23403G, S-D614G	E484Q E484G N501I A475S N439K G496C S494L A475V G446V S477I S477N F490L Q506K N487I F490V N501Y L455F N487D N437I Q493L T478K P499S
GH	B.1*	C241T, C3037T, A23403G, G25563T, S-D614G + NS3-Q57H	N501T E484Q K417N G504Y T478I N501Y E484K N439K T478K S494P G446V S477I S477N
GR	B.1.1.1	C241T, C3037T, A23403G, G25563T, S-D614G + N-G204R	N501T Y505H V445I L455F N501Y E484K T478K A475V S494P F490S S477R F490L S477N S477I
GV	B.1.177	C241T, C3037T, A23403G, C2222T, S-D614G + S-A222V	E484Q E484G N501I A475S N439K G496C S494L A475V G446V S477I S477N F490L Q506K N487I F490V N501Y L455F N487D N437I Q493L T478K P499S

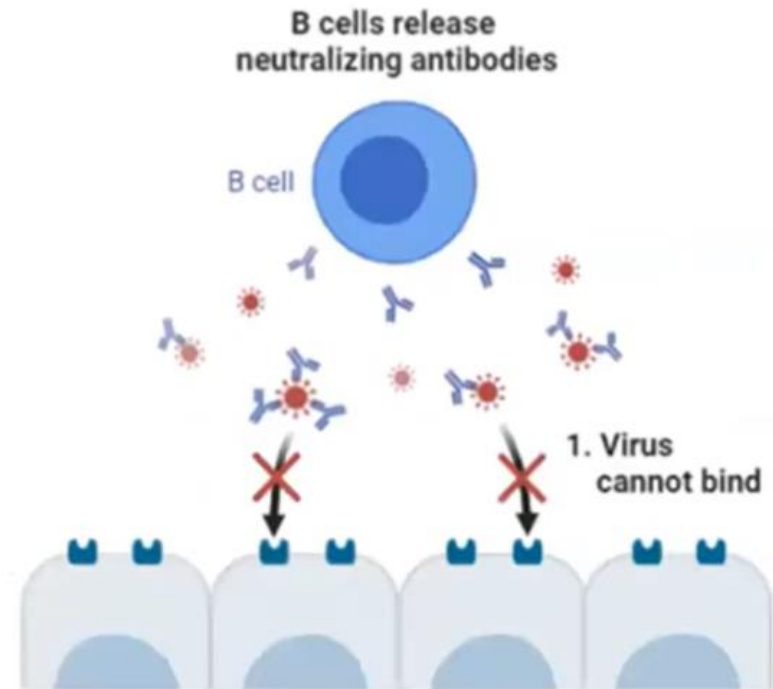
Source: GISAID. Available at: <https://platform.gisaid.org> Accessed on 11 January 2021.

SARS-CoV-2 Genetic Characterization

- To escape the immune response (natural or by vaccine)



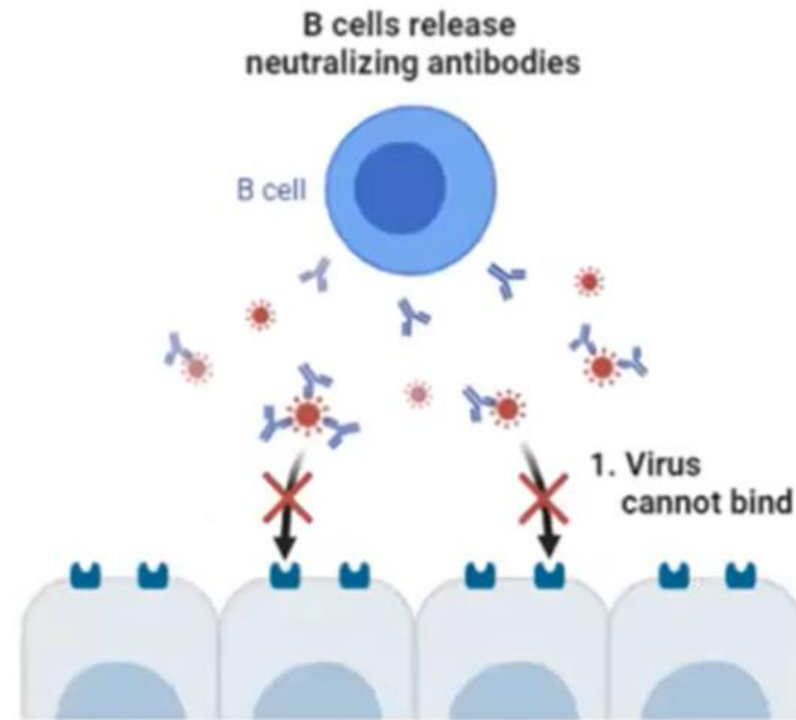
<https://www.clinicalomics.com/topics/patient-care/coronavirus/research-may-explain-why-men-are-more-susceptible-to-covid-19-than-women/>



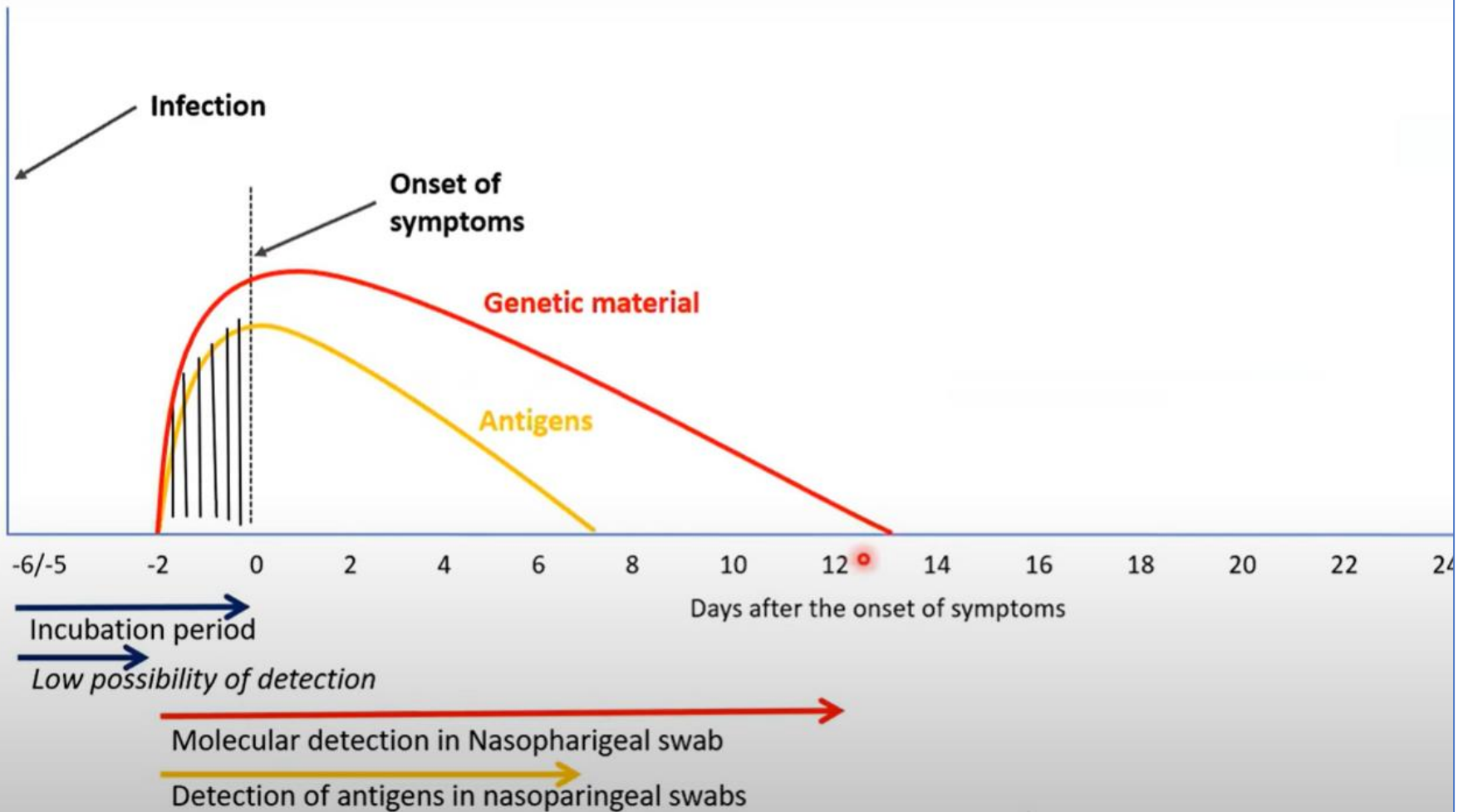
SARS-CoV-2 Genetic Characterization

- To escape the immune response (natural or by vaccine)

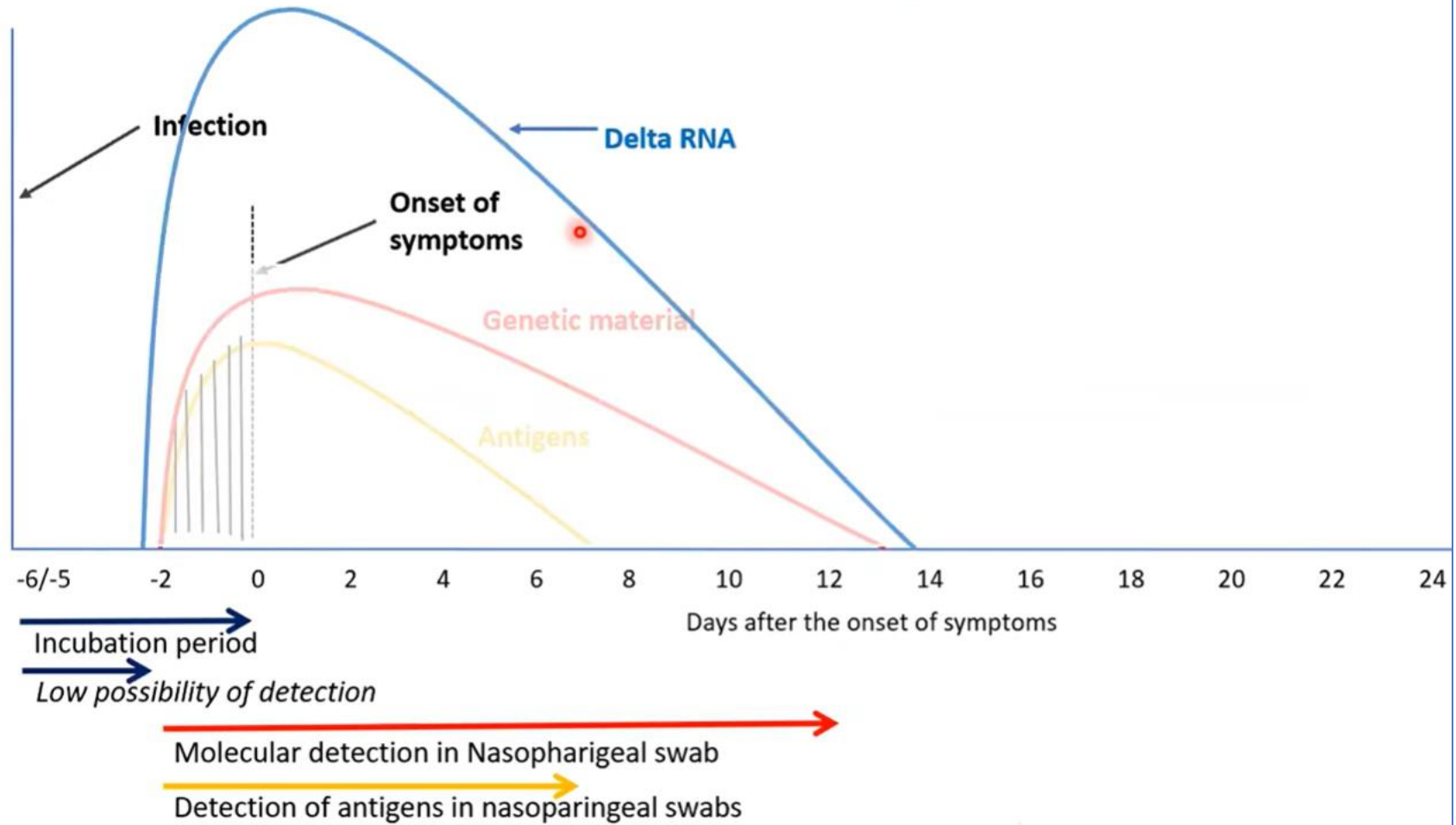
Some mutations can change the structure enough for the antibodies no to longer recognize the protein...



SARS-CoV-2 infection dynamics



SARS-CoV-2 infection dynamics



Variante de interés ó Variant of Interest (VOI) y Variante prioritarias ó Variant of Concern (VOC)

Variantes de interés (VOI): su genoma presenta mutaciones que llevan a cambios de aminoácidos asociados a cambios fenotípicos establecidos con respecto a la referencia.

Variante prioritaria (VOC): es una variante de interés en la que se demuestra a través de diferentes estrategias de análisis que:

- a) está asociada a un aumento de transmisibilidad o empeoramiento de la situación epidemiológica en la región;
- b) está asociada a un aumento de virulencia o cambio en la presentación clínica;
- c) está asociada a una disminución en la efectividad de las medidas de control, los tests diagnósticos, las vacunas o los tratamientos.

Larger clades in GISAID were named in context of marker variants relative to WIV04-reference:

S C8782T,T28144C NS8-L84S
 L C241,C3037,A23403,C8782,G11083,G25563,G26144,T28144,G28882 (WIV04-reference)
 V G11083T,G26144T NSP6-L37F + NS3-G251V
 G C241T,C3037T,A23403G S-D614G
 GK C241T,C3037T,A23403G,C22995A S-D614G + S-T478K
 GH C241T,C3037T,A23403G,G25563T S-D614G + NS3-Q57H
 GV C241T,C3037T,A23403G,C22227T S-D614G + S-A222V
 GR C241T,C3037T,A23403G,G28882A S-D614G + N-G204R
 GRY C241T,C3037T,21765-21770del,21991-21993del,A23063T,A23403G,G28882A includes S-H69del, S-V70del, S-Y144del, S-N501Y + S-D614G + N-G204R

Clade references and Pango lineages

GK_Delta__B.1.617.2__hCoV-19_India_ILSGS00941_2020_EPI_ISL_1663516_2020-12-12
 GRY_Alpha__B.1.1.7__hCoV-19_England_MIU-9E05B3_2020_EPI_ISL_601443_2020-09-20
 GR__B.1.1.1__hCoV-19_England_20168037604_2020_EPI_ISL_466615_2020-02-16
 GV__B.1.177__hCoV-19_Spain_CT-ISCIII-2019597_2020_EPI_ISL_539548_2020-06-26
 GH__B.1__hCoV-19_Canada_ON-PHL-8751_2020_EPI_ISL_418345_2020-02-02
 G__B.1__hCoV-19_Germany_BY-CHVIR-929_2020_EPI_ISL_406862_2020-01-28
 V__B.2__hCoV-19_Italy_LAZ-INMI-SPL1_2020_EPI_ISL_412974_2020-01-29
 L__B__hCoV-19_Wuhan_WIV04_2019_EPI_ISL_402124_2019-12-30
 S__A__hCoV-19_Guangdong_20SF012_2020_EPI_ISL_403932_2020-01-14

Sampled genome tree derived from all outbreak sequences

2021-09-07

Notable changes
 3,033,978 full genomes (+97,328)
 (excluding low coverage, out of 3,303,866 entries)

Updated clades
RBDx: relevant changes near receptor and antibody binding sites

- S clade [#RBDx] 13,716 [4,228] (+45 [+45])
- L clade [#RBDx] 5,502 [65] (+1 [+0])
- V clade [#RBDx] 6,533 [20] (+0 [+0])
- G clade [#RBDx] 206,645 [80,862] (+1,791 [+819])
- GR clade [#RBDx] 388,784 [187,663] (+2,452 [+2,056])
- GRY clade [#RBDx] 967,702 [66,736] (+11,391 [+594])
- GH clade [#RBDx] 412,567 [180,089] (+1,774 [+1,253])
- GV clade [#RBDx] 164,074 [4,473] (+288 [+52])
- GK clade [#RBDx] 848,884 [31,444] (+77,926 [+3,267])
- Other clade [#RBDx] 19,571 [9,872] (+1,660 [+1,591])

We gratefully acknowledge the Authors from Originating and Submitting laboratories of sequence data on which the analysis is based.



by BII/GIS, A*STAR Singapore

Blue: Asia
 Green: new from Oceania
 Magenta: new from Americas
 Red: new from Europe
 Yellow: new from Africa
 Grey: from previous updates

GK
Delta

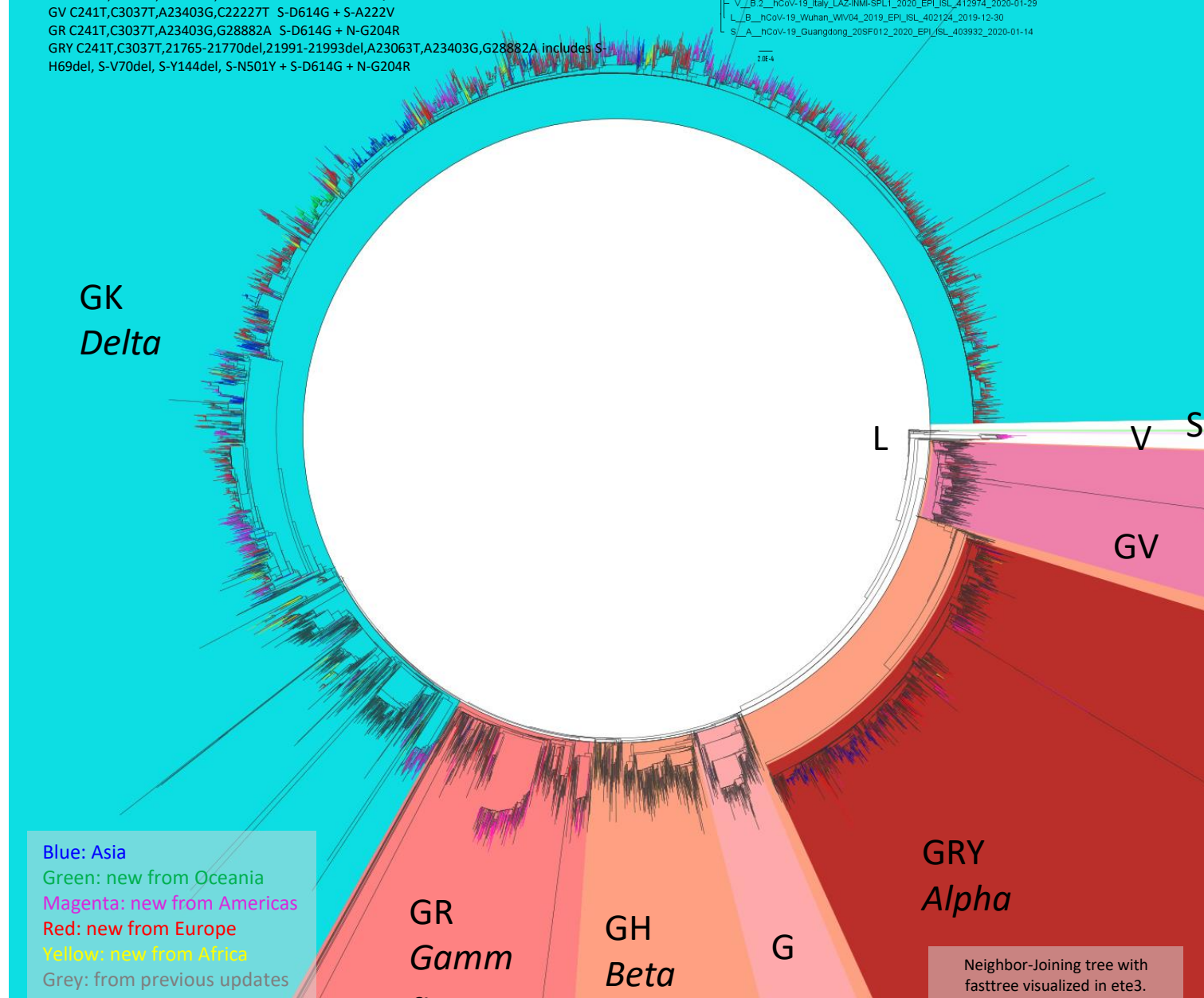
GR
Gamma

GH
Beta

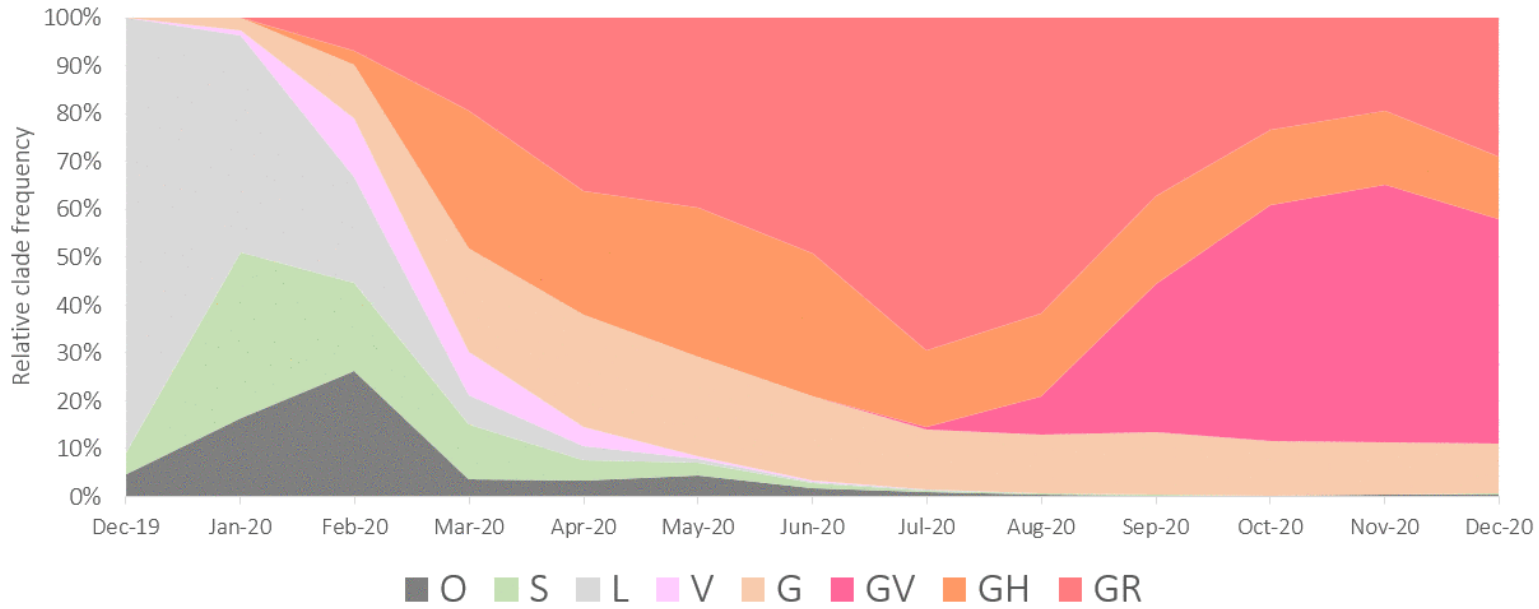
G

GRY
Alpha

Neighbor-Joining tree with fasttree visualized in ete3.



Clade evolution in the first year



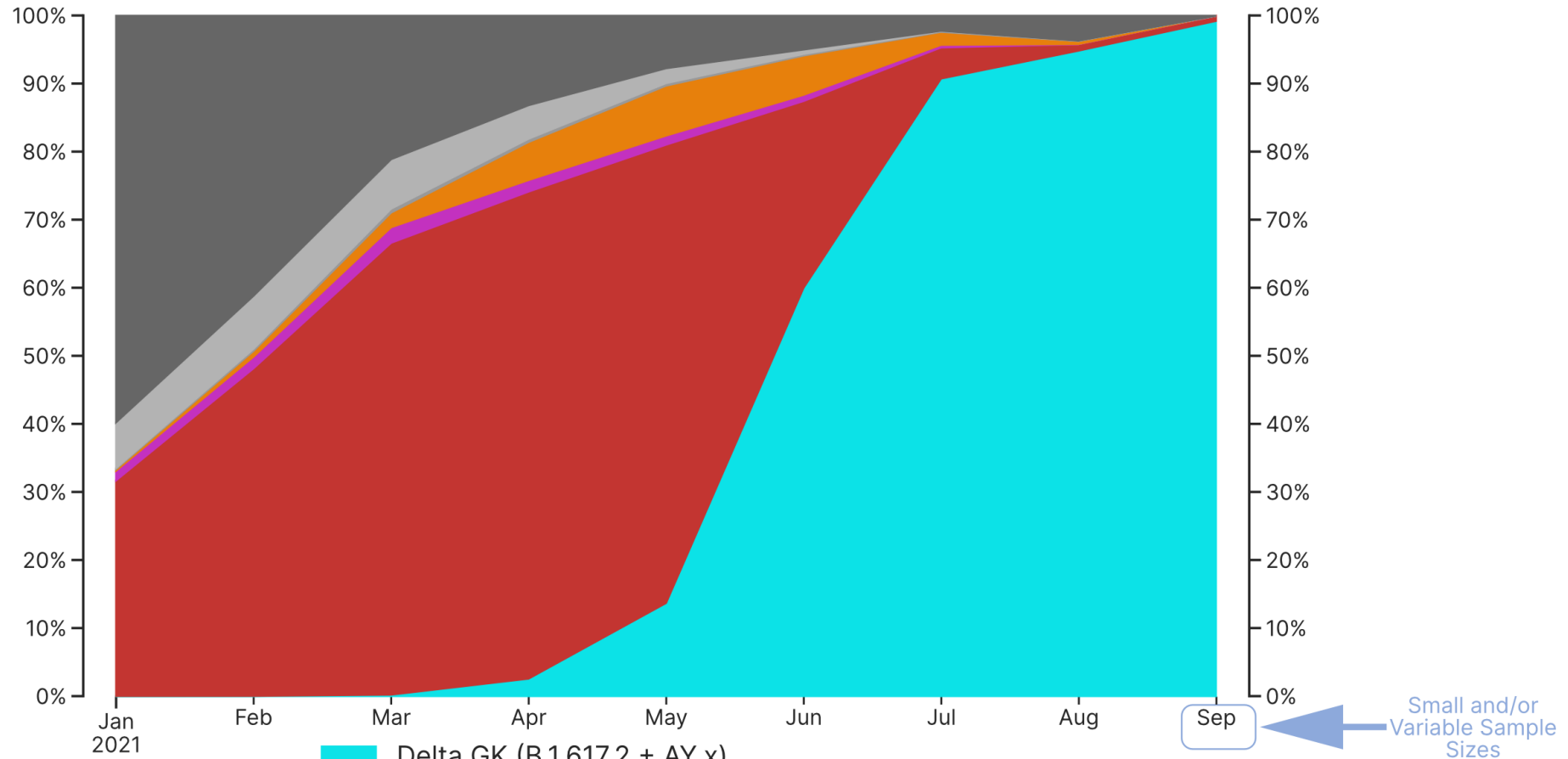
┆
0.000050

GISAID clades and
PANGO lineages

by BII/GIS, A*STAR
Singapore



Timecourse of variant distribution in all submitted sequences 2021-09-07

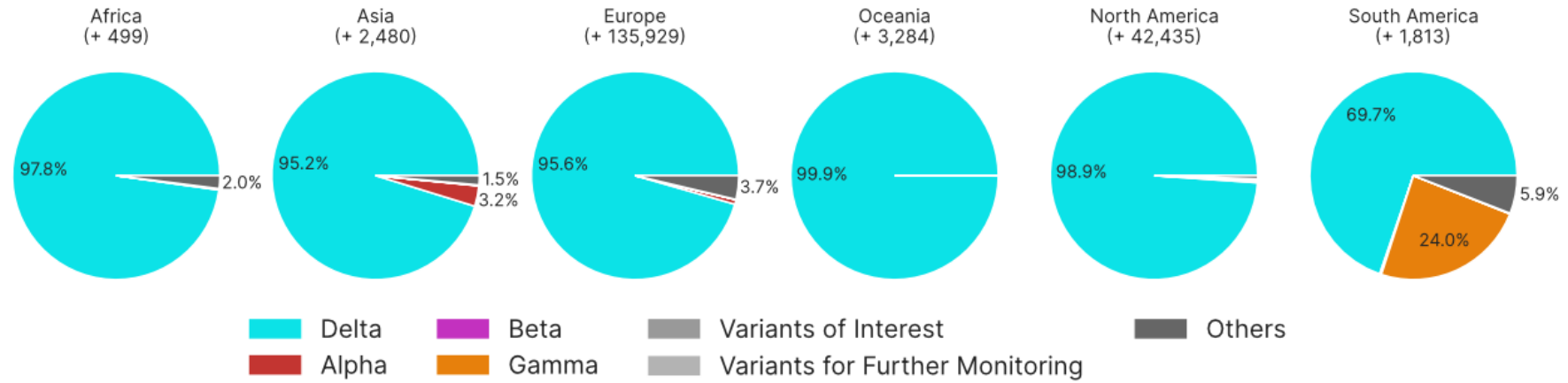


- Delta GK (B.1.617.2 + AY.x)
- Alpha GRY (B.1.1.7)
- Beta GH/501Y.V2 (B.1.351 + B.1.351.2 + B.1.351.3)
- Gamma GR/501Y.V3 (P.1 + P.1.x)
- Variants of Interest
- Variants for Further Monitoring
- Others

We gratefully acknowledge the Authors from Originating and Submitting laboratories of sequence data on which the analysis is based.



Regional distribution of variants in sequences collected from 2021-08-10 to 2021-09-07



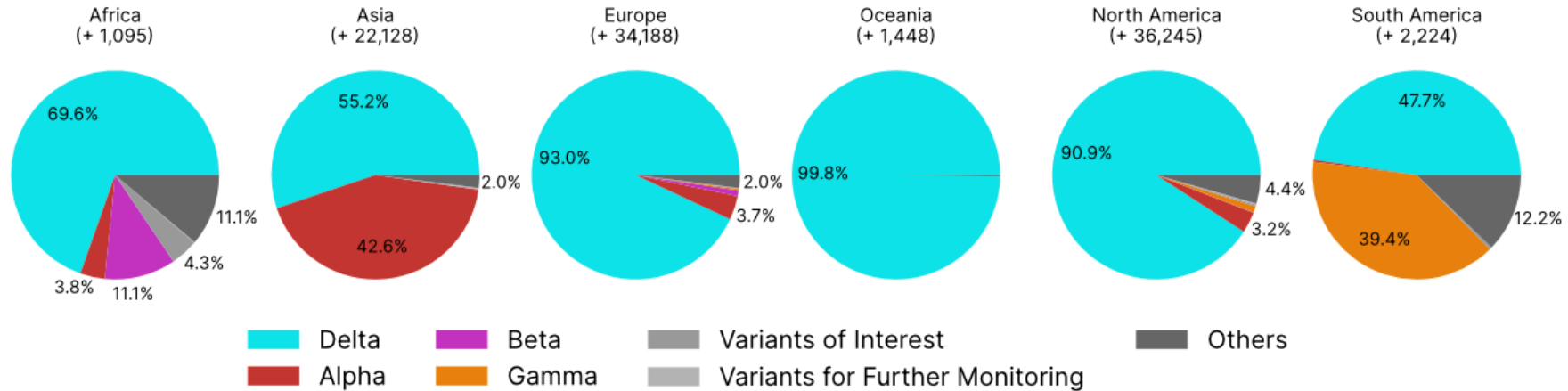
Change in proportions of variants compared to the four weeks before 2021-08-10

	Africa	Asia	Europe	Oceania	North America	South America
Delta	+6.8%	+16.3%	+0.2%	+0.3%	+3.4%	+22.1%
Alpha	-0.3%	-13.6%	-0.8%	-0.1%	-1.1%	-0.7%
Beta	-3.6%	-0.0%	-0.1%	+0.0%	-0.0%	+0.1%
Gamma	+0.0%	+0.0%	-0.2%	+0.0%	-0.7%	-16.9%
Variants of Interest	+0.0%	+0.0%	-0.0%	+0.0%	-0.1%	-0.1%
Variants for Further Monitoring	+0.0%	-0.0%	-0.0%	+0.0%	-0.0%	+0.1%
Others	-2.9%	-2.6%	+0.9%	-0.2%	-1.5%	-4.5%

See <https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/> for variant information and definitions



Regional distribution of variants in new sequences 2021-09-07



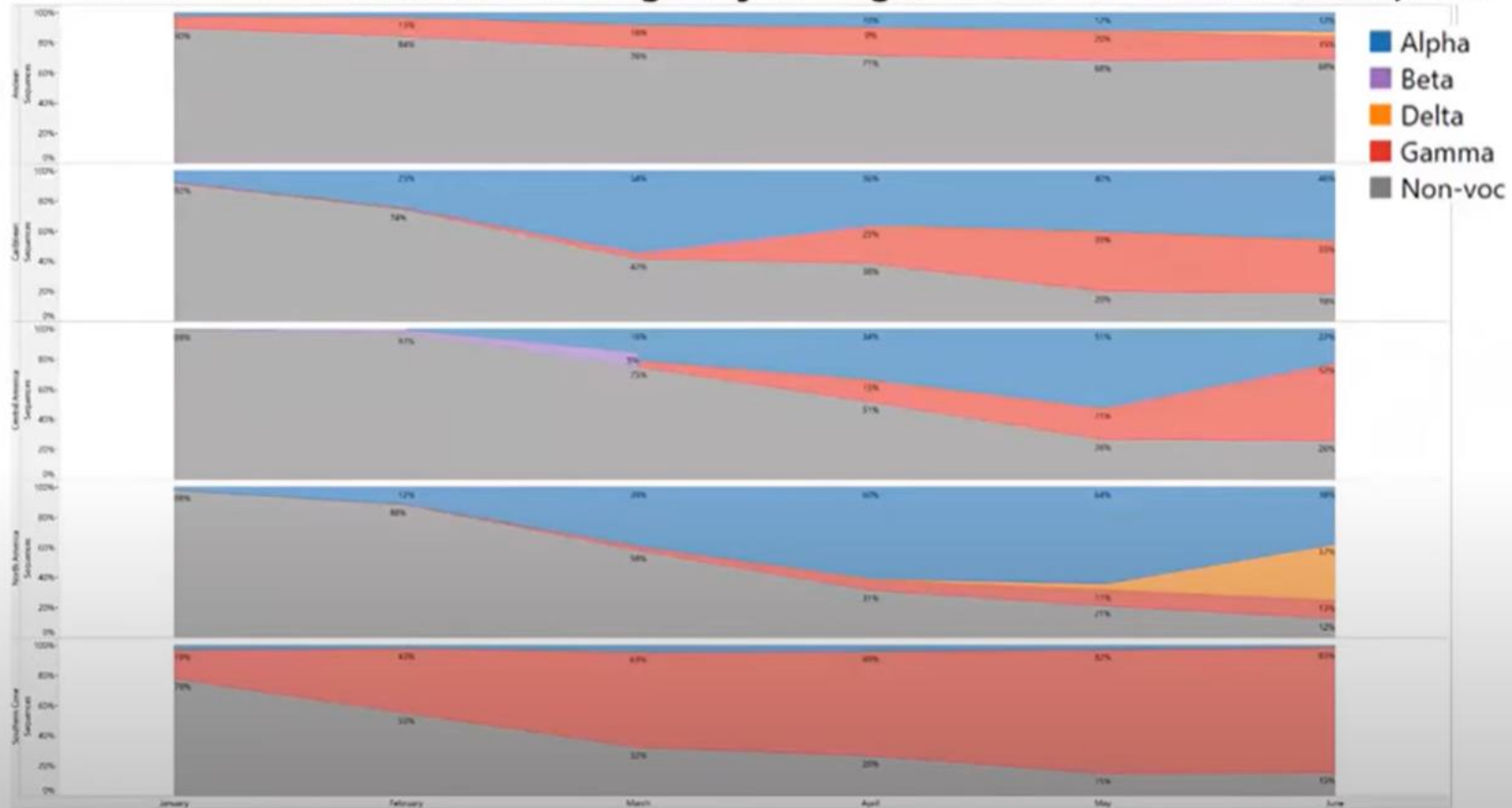
	<i>Africa</i>	<i>Asia</i>	<i>Europe</i>	<i>Oceania</i>	<i>North America</i>	<i>South America</i>
% Delta G/478K.V1 (B.1.617.2 + AY.x)	69.6	55.2	93.0	99.8	90.9	47.7
% Alpha GRY/501Y.V1 (B.1.1.7)	3.8	42.6	3.7	0.0	3.2	0.3
% Beta GH/501Y.V2 (B.1.351 + B.1.351.1 + B.1.351.2)	11.1	0.0	0.9	0.0	0.0	0.0
% Gamma GR/501Y.V3 (P.1 + P.1.x)	0.0	0.0	0.2	0.0	1.0	39.4
% Variants of Interest	4.3	0.0	0.1	0.0	0.3	0.4
% Variants for Further Monitoring	0.1	0.3	0.1	0.0	0.2	0.0
% Other Variants	11.1	2.0	2.0	0.2	4.4	12.2

This slide shows NEW data in GISAID on 2021-09-07 submitted since last report 4 days ago (new by submission date, not collection date)
 See <https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/> for variant information and definitions



SARS-CoV-2 Variants of Concern (VOC)

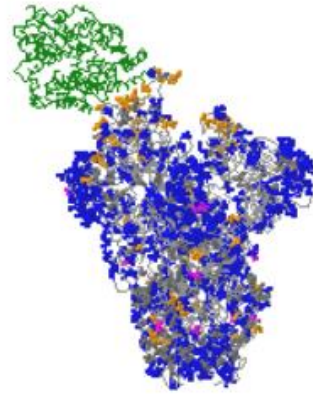
Distribution of SARS-CoV-2 lineages by subregion & month—The Americas, 2021



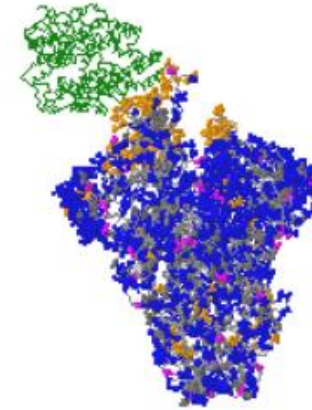
Receptor binding surveillance for complete genomes 2021-09-07

Changes in the spike glycoprotein for the 97,328 new complete genomes.

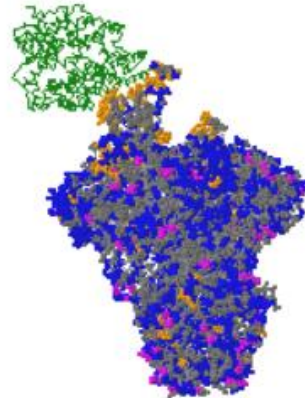
N501T E484Q K417N K417T N501Y E484K Y449N N439K
S494L T478K A475V S494P F490S Q493K S477I S477N
in GH clade (B.1.*)



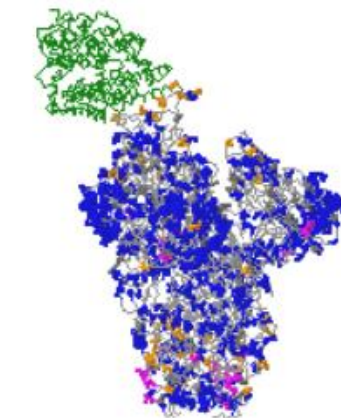
E484Q Y449H F456L G446V S477N Y495H F490L
F486L N501T Y505N N501Y G447V E484K G447C
G447S K417R G485R T478K S494P Q493R E484G
K417N V503F Y453F N439K Y449S A475V F490S
G485V Y489H K417T G485D V445I L455F E484D
G485A
in GR & GRY clade (B.1.1.1 & B.1.1.7)



G504L E484Q Y473H T478I A475T G504C G504S K458M
S477N G476S S494A N501Y N487D V503A E484K E484V
K417R K458N Q493L E484G G504V G504D V503F Y453F
E484A Q493E K417E V503I G485V Q493P K417T G485S
G446S N501S V445F K458R G496V G502E V445A R403S
V503Y S494L Q493H G446V F456L F490L N501T T478R
G446A N437S T478K G485R S494P L455S Q498R P499T
K417N N501I A475S G446F N439K S477G G476R A475V
S477R F490S S477I S477V F490V N439I V445I L455F E484D
G485A G446D G502S P499S V503G R403I
in G, GK & GV clades (B.1, B.1.617.2, AY.* & B.1.177)



N501T K417N E484Q K417T N501Y E484A E484K S477G
T478K S494L A475V F490S S477N
in nonG clade (A, B & B.2)



Green ... ACE2 human host receptor

Gray ... CoV spike glycoprotein trimer

Gray balls ... Spike glycoprotein variation occurring 100 times or less

Blue balls ... Spike glycoprotein variation occurring greater than 100 times

Red balls ... Spike glycoprotein variation near host receptor with effect history

Orange balls ... Spike glycoprotein variation near host receptor, or other functional annotation

Cyan ... Insertion/deletion

Magenta balls ... Spike glycoprotein variation altering potential N-glycosylation sites

*We gratefully acknowledge
the Authors from Originating
and Submitting laboratories
of sequence data on which the
analysis is based.*

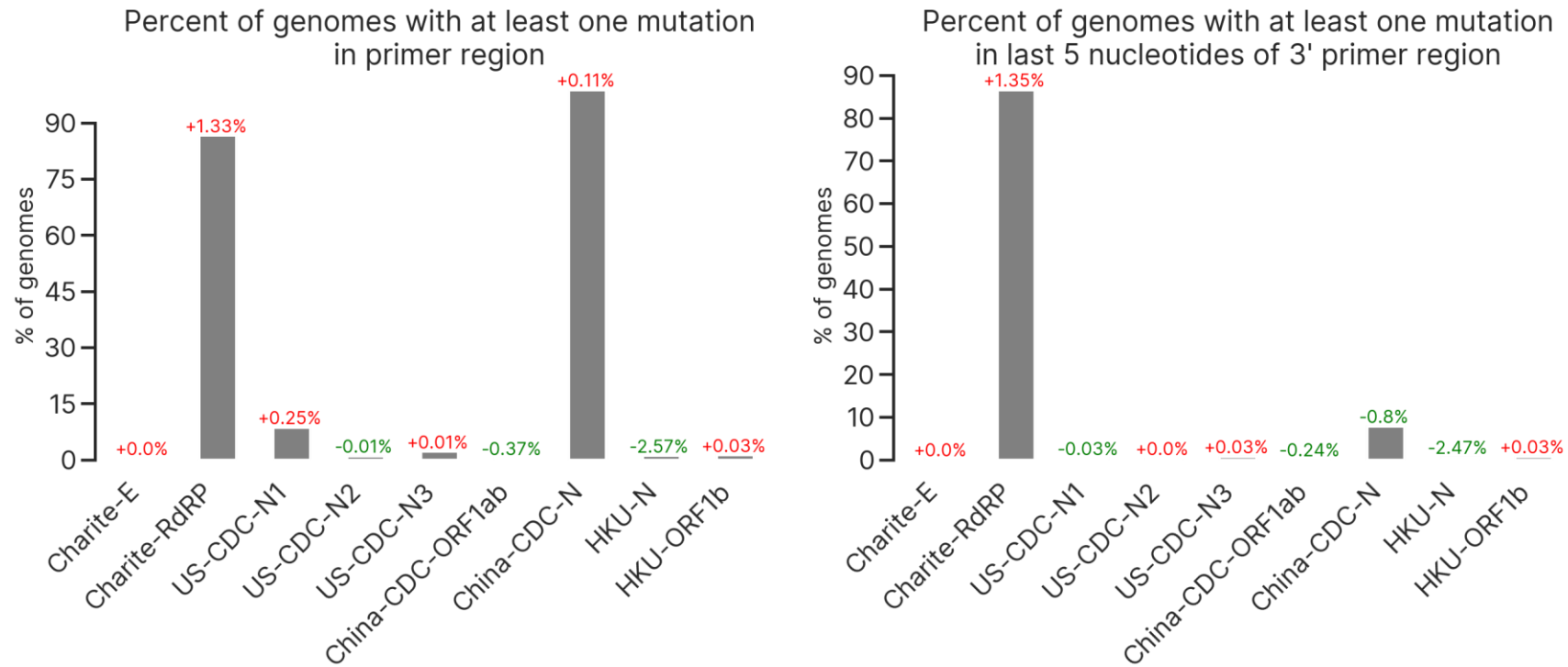
Equivalent positions have been studied for V483A and V483I in MERS (DOI: 10.1128/JVI.01381-18) and G476S, L455I, F456L, F456V, S494P, A475V, N439K, K444R and V503F in SARS (DOI: 10.1074/jbc.M111.325803 DOI: 10.1086/651022 DOI:10.1186/1743-422X-2-73 DOI:10.1093/molbev/msq056)

where they most often weakly reduced host receptor binding and altered antigenicity. Numbering relative to start codon 21563 in hCoV-19/Wuhan/WIV04/2019



by BII/GIS, A*STAR Singapore

Common Primer Check for High Quality Genomes 2021-09-07



To reduce noise of random mutations ~ 693,784 available high quality genomes (out of 710,884 entries) **submitted in the past 90 days** are considered here. Each bar is annotated with the change in percentage since the previous update.

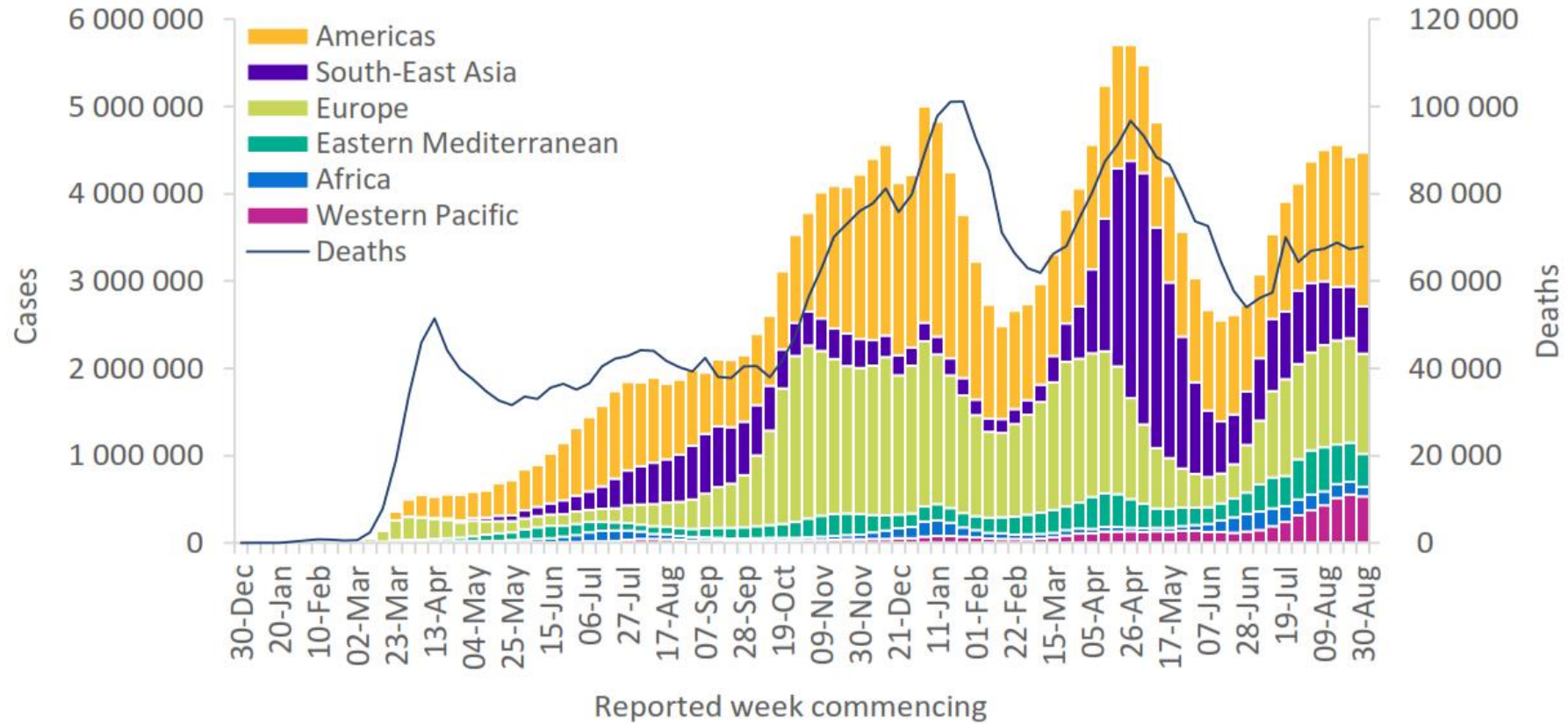
This is a simplified summary view of the percent of high quality genomes (defined as <1% Ns and <0.05% unique non-synonymous mutations) with one or more mutations in either forward, probe or reverse primer region. This does not necessarily indicate a primer would not function but serves as a guide to variability of the targeted region. The second Figure shows the same but with mutations in 3' ends for the primer regions (defined as last 5 nucleotides of the primer sequence) which can affect sensitivity partially.

Sources of primer sequences (may have been updated in meantime): <https://www.who.int/docs/default-source/coronaviruse/protocol-v2-1.pdf>
<https://www.who.int/docs/default-source/coronaviruse/peiris-protocol-16-1-20.pdf>
http://ivdc.chinacdc.cn/kjz/202001/t20200121_211337.html
<https://www.who.int/docs/default-source/coronaviruse/uscdcr-pcr-panel-primer-probes.pdf>



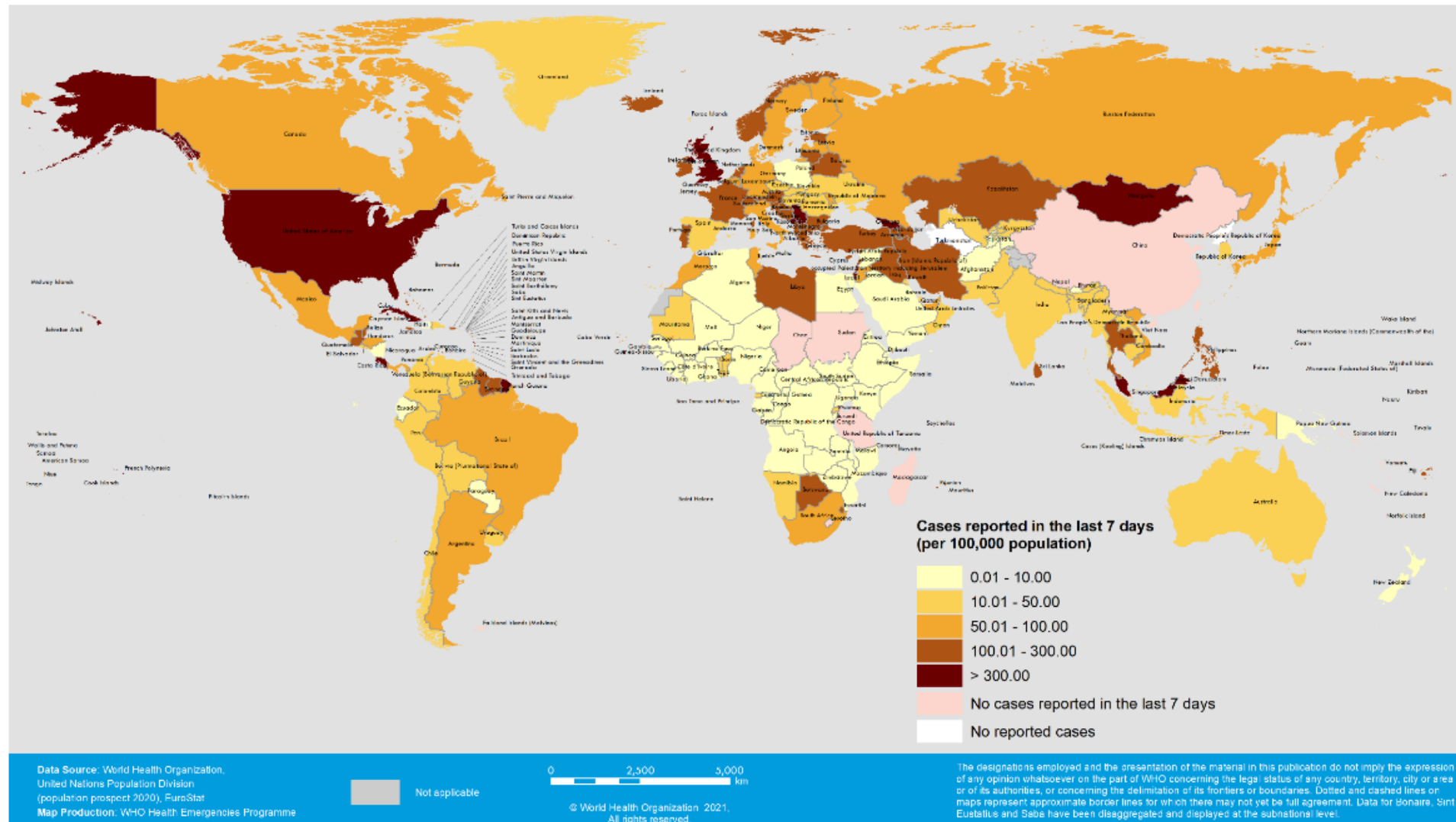
by BII/GIS, A*STAR Singapore

Figure 1. COVID-19 cases reported weekly by WHO Region, and global deaths, as of 5 September 2021**



**See [Annex 2: Data, table and figure notes](#)

Figure 2. COVID-19 cases per 100 000 population reported by countries, territories and areas, 30 August – 5 September 2021**



**See Annex 2: Data, table and figure notes

Variants of Concern (VOC)

Working definition:

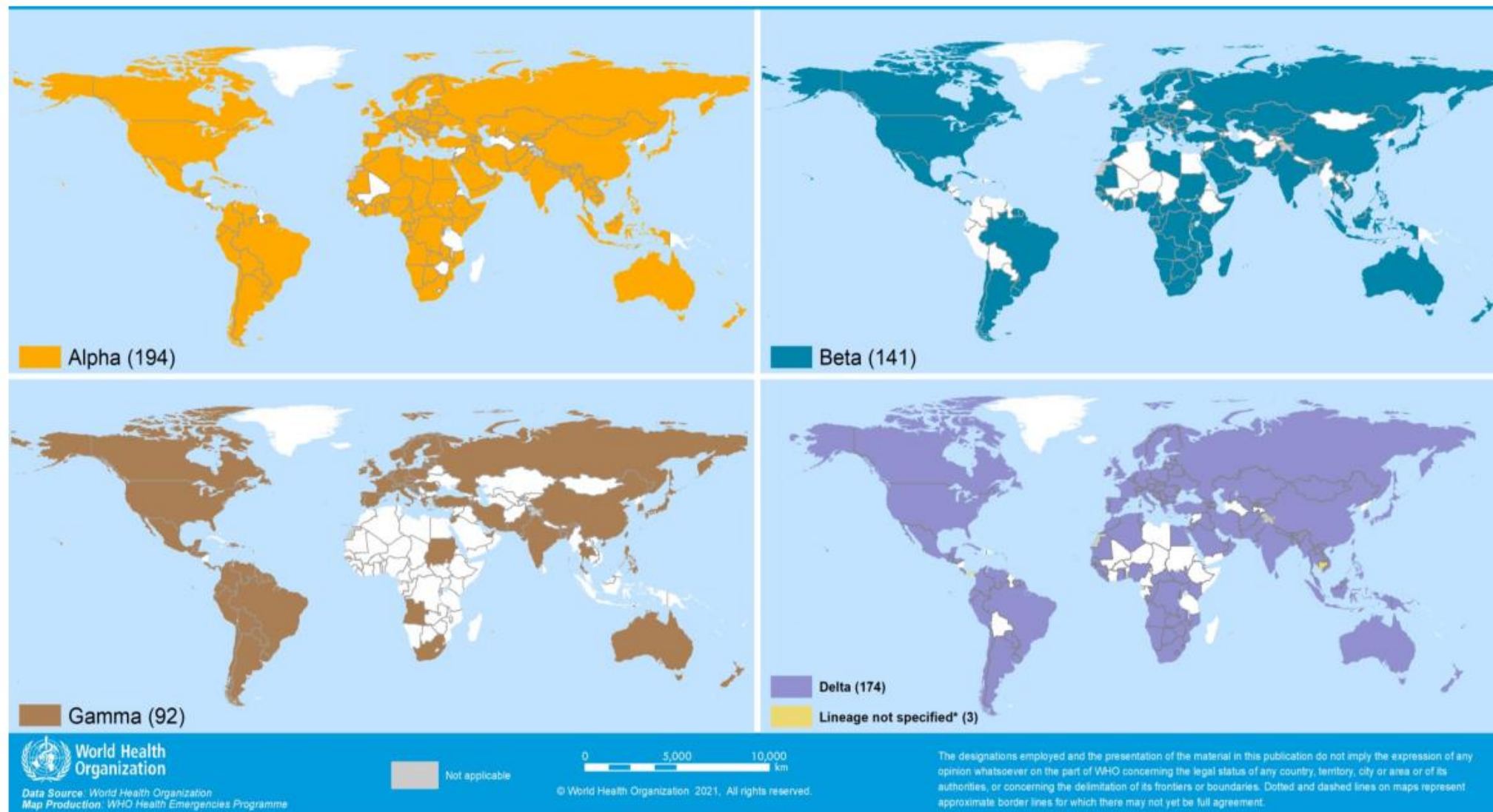
A SARS-CoV-2 variant that meets the definition of a VOI (see below) and, through a comparative assessment, has been demonstrated to be associated with one or more of the following changes at a degree of global public health significance:

- 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.

Currently designated Variants of Concern:

WHO label	Pango lineage*	GISAID clade	Nextstrain clade	Additional amino acid changes monitored°	Earliest documented samples	Date of designation
Alpha	B.1.1.7 #	GRY	20I (V1)	+S:484K +S:452R	United Kingdom, Sep-2020	18-Dec-2020
Beta	B.1.351	GH/501Y.V2	20H (V2)	+S:L18F	South Africa, May-2020	18-Dec-2020
Gamma	P.1	GR/501Y.V3	20J (V3)	+S:681H	Brazil, Nov-2020	11-Jan-2021
Delta	B.1.617.2§	G/478K.V1	21A	+S:417N	India, Oct-2020	VOI: 4-Apr-2021 VOC: 11-May-2021

Figure 4. Countries, territories and areas reporting variants Alpha, Beta, Gamma and Delta, as of 7 September 2021**



*Includes countries/territories/areas reporting the detection of B.1.617 without further specification of lineage at this time. These will be reallocated as further details become available.

**Countries/territories/areas highlighted include both official and unofficial reports of VOC detections, and do not presently differentiate between detections among travellers (e.g., at Points of Entry) or local community cases. Please see Annex 2 for further details.

Variants of Interest (VOI)

Working definition

A SARS-CoV-2 variant :

- with genetic changes that are predicted or known to affect virus characteristics such as transmissibility, disease severity, immune escape, diagnostic or therapeutic escape; AND
- Identified to cause significant community transmission or multiple COVID-19 clusters, in multiple countries with increasing relative prevalence alongside increasing number of cases over time, or other apparent epidemiological impacts to suggest an emerging risk to global public health.

Currently designated Variants of Interest:

WHO label	Pango lineage*	GISAID clade	Nextstrain clade	Earliest documented samples	Date of designation
Eta	B.1.525	G/484K.V3	21D	Multiple countries, Dec-2020	17-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	21G	Peru, Dec-2020	14-Jun-2021
Mu	B.1.621	GH	21H	Colombia, Jan-2021	30-Aug-2021

*includes all descendent lineages. The full list of Pango lineages can be found here:https://cov-lineages.org/lineage_list.html; for FAQ, visit: <https://www.pango.network/faqs/>

Nextstrain - Nivel global

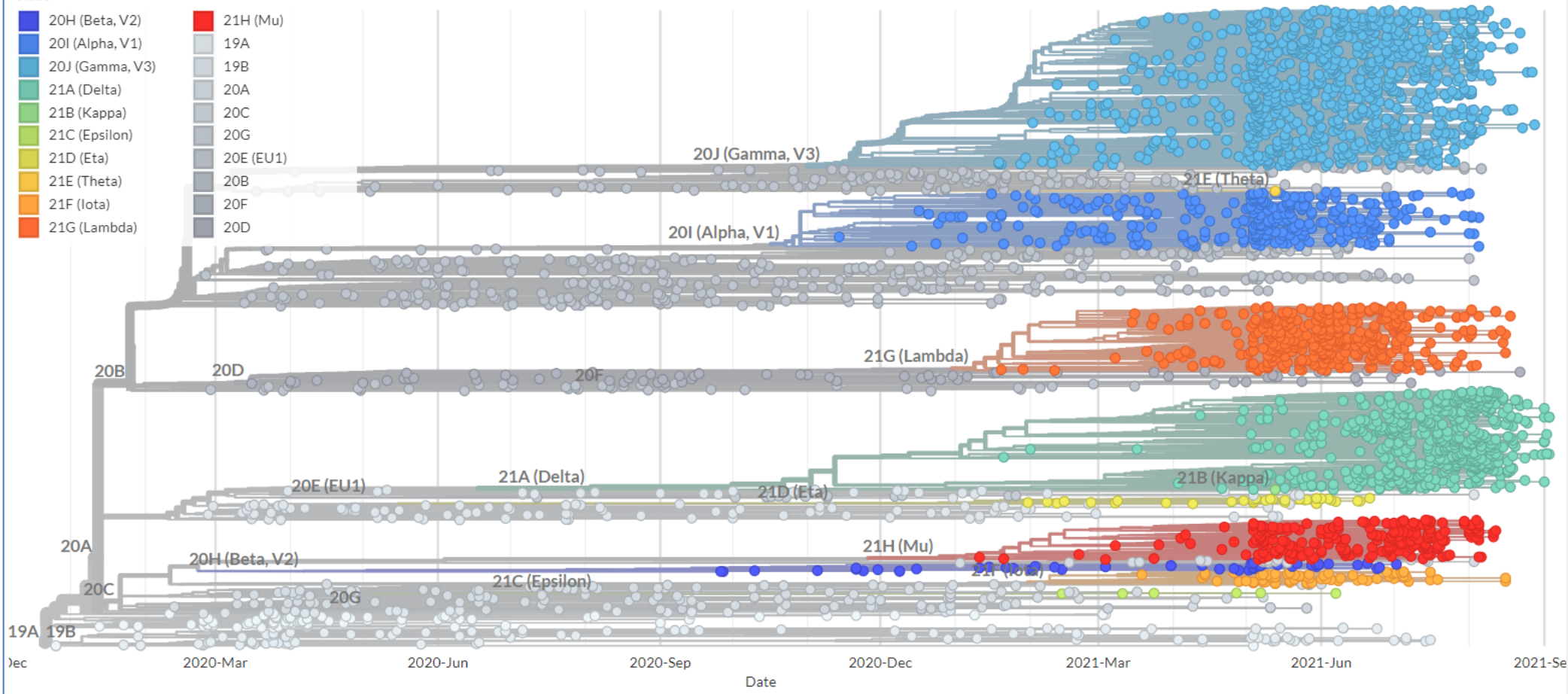
Showing 3591 of 3591 genomes sampled between Dec 2019 and Sep 2021.

Phylogeny

Clade ^

- 20H (Beta, V2)
- 20I (Alpha, V1)
- 20J (Gamma, V3)
- 21A (Delta)
- 21B (Kappa)
- 21C (Epsilon)
- 21D (Eta)
- 21E (Theta)
- 21F (Iota)
- 21G (Lambda)
- 21H (Mu)
- 19A
- 19B
- 20A
- 20C
- 20G
- 20E (EU1)
- 20B
- 20F
- 20D

ZOOM TO SELECTED RESET LAYOUT



Reclassifying VOIs/ VOCs

A previously designated Variant of Interest (VOI) or Variant of Concern (VOC) which has conclusively demonstrated to no longer pose a major added risk to global public health compared to other circulating SARS-CoV-2 variants, can be reclassified.

This is undertaken through a critical expert assessment, in collaboration with Technical Advisory Group on Virus Evolution, of several criteria, such as the observed incidence/relative prevalence of variant detections among sequenced samples over time and between geographical locations, the presence/absence of other risk factors, and any ongoing impact on control measures.

Alerts for Further Monitoring

Working definition

A SARS-CoV-2 variant with genetic changes that are suspected to affect virus characteristics with some indication that it may pose a future risk, but evidence of phenotypic or epidemiological impact is currently unclear, requiring enhanced monitoring and repeat assessment pending new evidence.

Note: It is expected that our understanding of the impacts of these variants may fast evolve, and designated Alerts for Further Monitoring may be readily added/removed; therefore, WHO labels will not be assigned at this time. Former VOIs/VOCs may, however, be monitored for an extended period under this category, and will maintain their assigned WHO label until further notice.

Currently designated Alerts for Further Monitoring:

Pango lineage*	GISSAID clade	Nextstrain clade	Earliest documented samples	Date of designation
B.1.427 B.1.429	GH/452R.V1	21C	United States of America, Mar-2020	VOI: 5-Mar-2021 Alert: 6-Jul-2021
R.1	GR	-	Multiple countries, Jan-2021	07-Apr-2021
B.1.468.2	GH	-	Indonesia, Nov-2020	28-Apr-2021
B.1.1.318	GR	-	Multiple countries, Jan-2021	02-Jun-2021
B.1.1.519	GR	20B/S.732A	Multiple countries, Nov-2020	02-Jun-2021
C.36.3	GR	-	Multiple countries, Jan-2021	16-Jun-2021
B.1.214.2	G	-	Multiple countries, Nov-2020	30-Jun-2021
B.1.1.523	GR	-	Multiple countries, May-2020	14-July-2021
B.1.619	G	20A/S.126A	Multiple countries, May-2020	14-July-2021
B.1.620	G	-	Multiple countries, November 2020	14-July-2021
C.1.2	GR	-	South Africa, May 2021	01-Sep-2021

*includes all descendent lineages. The full list of Pango lineages can be found here: https://cov-lineages.org/lineage_list.html; for FAQ, please visit: <https://www.pango.network/faqs/>

Table 2: Summary of phenotypic impacts* of Variants of Concern

WHO label	Alpha	Beta	Gamma	Delta
Transmissibility	Increased transmissibility ⁵	Increased transmissibility ^{6,7}	Increased transmissibility ^{7,8}	Increased transmissibility and secondary attack rate ^{7,9}
Disease severity	Increased risk of hospitalization ¹⁰ , possible increased risk of severity and mortality ^{11,2}	Not confirmed, possible increased risk of in-hospital mortality ¹²	Not confirmed, possible increased risk of hospitalization ¹³	Increased risk of hospitalization ¹⁴
Risk of reinfection	Neutralizing activity retained ¹⁵ , risk of reinfection remains similar ¹⁶	Reduction in neutralizing activity reported; T cell response elicited by D614G virus remains effective ¹⁷	Moderate reduction in neutralizing activity reported ¹⁸	Reduction in neutralizing activity reported ¹⁹⁻²¹
Impacts on diagnostics	Limited impact – S gene target failure (SGTF); no impact on overall result from multiple target RT-PCR, No impact on Ag RDTs observed ²²	No impact on RT-PCR or Ag RDTs observed ²¹	None reported to date	None reported to date

**Generalized findings as compared to previously/co-circulating variants. Based on emerging evidence, including non-peer-reviewed preprint articles and reports, all subject to ongoing investigation and revision.*

Table 3. Summary of vaccine performance against Variants of Concern

	Anhui ZL- Recombinant	AstraZeneca- Vaxzevria	Beijing CNIBG- BBIBP-CorV	Bharat-Covaxin	Gamaleya- Sputnik V	Janssen- Ad26.COV 2.5	Moderna- mRNA-1273	Moderna- mRNA-1273/ Pfizer BioNTech- Comirnaty	Novavax- Covavax	Pfizer BioNTech- Comirnaty	SII - Covishield	Sinovac- CoronaVac
Alpha^{23,24}												
Summary of VE*	Protection retained against all outcomes											
- Severe disease	-	↓ ₁	-	-	-	-	↔ ₁	↔ ₁	-	↔ ₄	-	-
- Symptomatic disease	-	↔ to ↓ ₃	-	-	-	-	↔ ₁	↔ ₁	↓ ₁	↔ ₃	-	-
- Infection	-	↔ to ↓ ₂	-	-	-	-	↔ ₁	-	-	↔ ₂	-	-
Neutralization	↔ ₂	↓ ₅	↔ ₁	↔ ₂	↔ ₃	↔ ₃	↔ to ↓ ₁₁	↓ ₁	↓ ₁	↔ to ↓ ₃₇	↔ ₁	↔ to ↓ ₅
Beta²⁵⁻²⁸												
Summary of VE*	Protection retained against severe disease; reduced protection against symptomatic disease; limited evidence											
- Severe disease	-	-	-	-	-	↔ ₁	-	-	-	↔ ₂	-	-
- Symptomatic disease	-	↓↓↓ ₁	-	-	-	↔ ₁	-	-	↓↓↓ ₁	↔ ₁	-	-
- Infection	-	-	-	-	-	-	↔ ₁	-	-	↓ ₁	-	-
Neutralization	↔ to ↓ ₃	↔ to ↓↓ ₆	↔ to ↓ ₂	↓ ₂	↓ to ↓↓ ₃	↓ to ↓↓ ₅	↓ to ↓↓ ₁₃	↓↓↓ ₁	↓↓↓ ₁	↓ to ↓↓ ₃₄	↓ ₁	↓ to ↓↓ ₄
Gamma												
Summary of VE*	Unclear impact; very limited evidence											
- Severe disease	-	-	-	-	-	-	-	-	-	-	-	-
- Symptomatic disease	-	-	-	-	-	-	-	-	-	-	-	-
- Infection	-	-	-	-	-	-	-	-	-	-	-	↔ ₁
Neutralization	↔ ₁	↓ ₂	-	-	↓ ₂	↓ ₂	↓ ₆	-	-	↔ to ↓ ₁₈	-	↔ to ↓ ₃
Delta²⁹												
Summary of VE*	Protection retained against severe disease; possible reduced protection against symptomatic disease and infection; limited evidence											
- Severe disease	-	↔ ₁	-	-	-	-	↔ ₁	-	-	↔ ₄	-	-
- Symptomatic disease	-	↓↓ ₂	-	↓ ₁	-	-	-	-	-	↔ to ↓ ₃	-	-
- Infection	-	↓ ₁	-	-	-	-	-	-	-	↓ ₁	-	-
Neutralization	↔ to ↓ ₂	↓ to ↓↓ ₅	-	↔ to ↓ ₃	↓ ₂	↓ ₃	↓ ₄	↓↓ ₁	-	↓ to ↓↓ ₁₀	↓ ₂	↓ to ↓↓ ₂

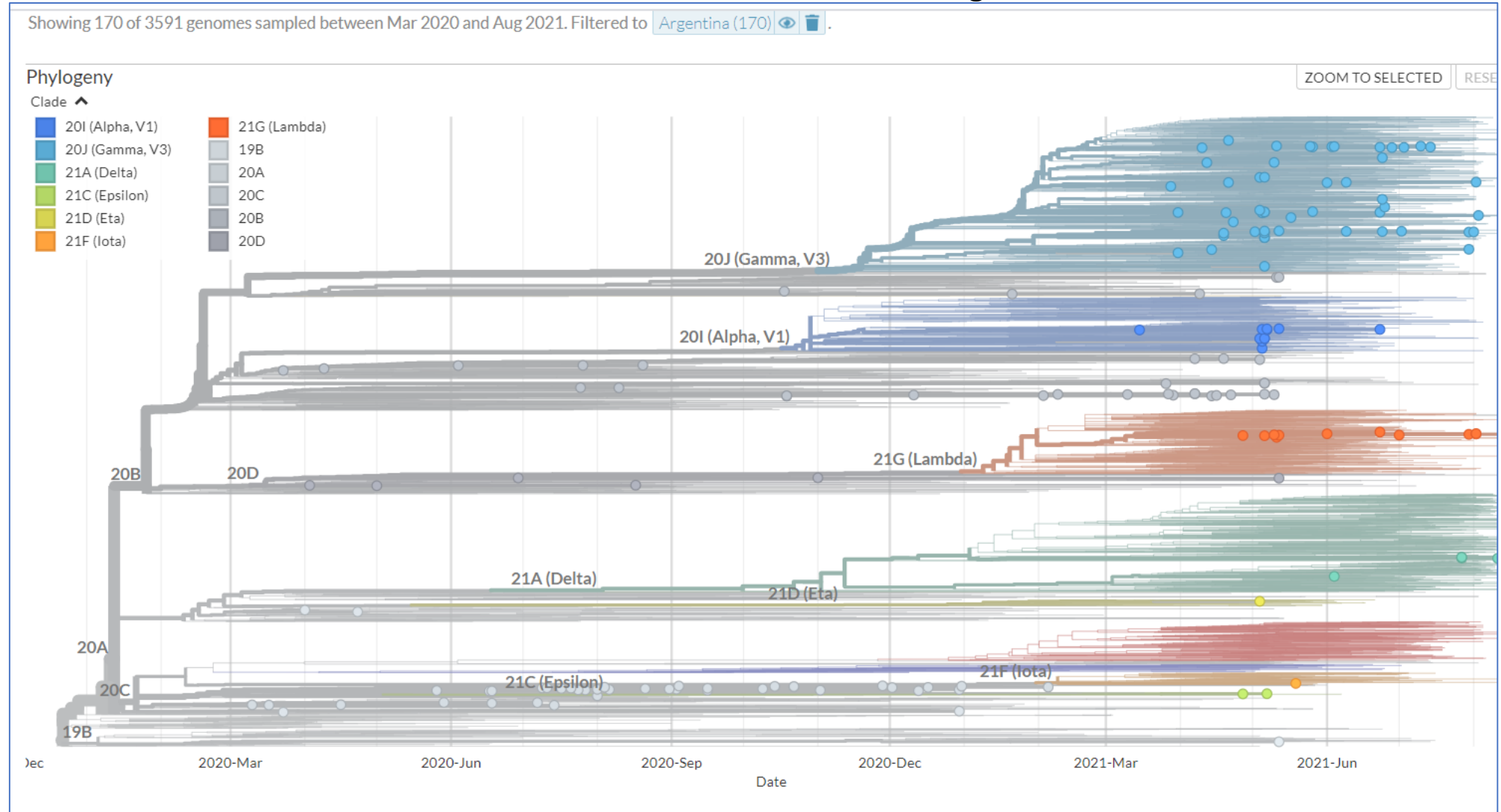
VE refers to vaccine effectiveness and vaccine efficacy

Summary of VE*: indicates the general conclusions but only for the vaccines evaluated against the specific variant

Arrows generalize the magnitude of reduction in VE or neutralization: "↔" <10% reduction in VE, or VE >90% with no comparator, or that there was a <2-fold reduction in neutralization; "↓" 10 to <20% reduction in VE, or 2 to <5-fold reduction in neutralization; "↓↓" 20 to <30% reduction in VE, or 5 to <10-fold reduction in neutralization; "↓↓↓" ≥30% reduction in VE, or ≥10-fold reduction in neutralization. When more than one neutralization study is available, the interquartile range (25th and 75th percentiles) of fold-reductions across all studies for specific vaccine/variant was used.

"Moderna-mRNA-1273/Pfizer BioNTech-Comirnaty" indicates that both vaccines were evaluated together in study.

Nextstrain - Argentina



Estrategia de Vigilancia genómica de SARS-CoV-2. Argentina

El Laboratorio Nacional de Referencia del INEI-ANLIS selecciona casos para secuenciación en los que se confirmó la presencia de SARS-CoV-2 según:

- Casos confirmados en nuestras provincias con antecedentes de viaje al exterior del país.
- Muestras de viajeros que resultan positivas en el tamizaje que se realiza en puntos de entrada al país.
- Casos confirmados en dos eventos separados para descartar/ confirmar reinfecciones.
- Casos confirmados con presentaciones clínicas severas y/o elevado incremento del numero de casos de manera inesperada.
- Casos confirmados en personas con esquemas completos de vacunación.



Methods for the detection and identification of SARS-CoV-2 variants

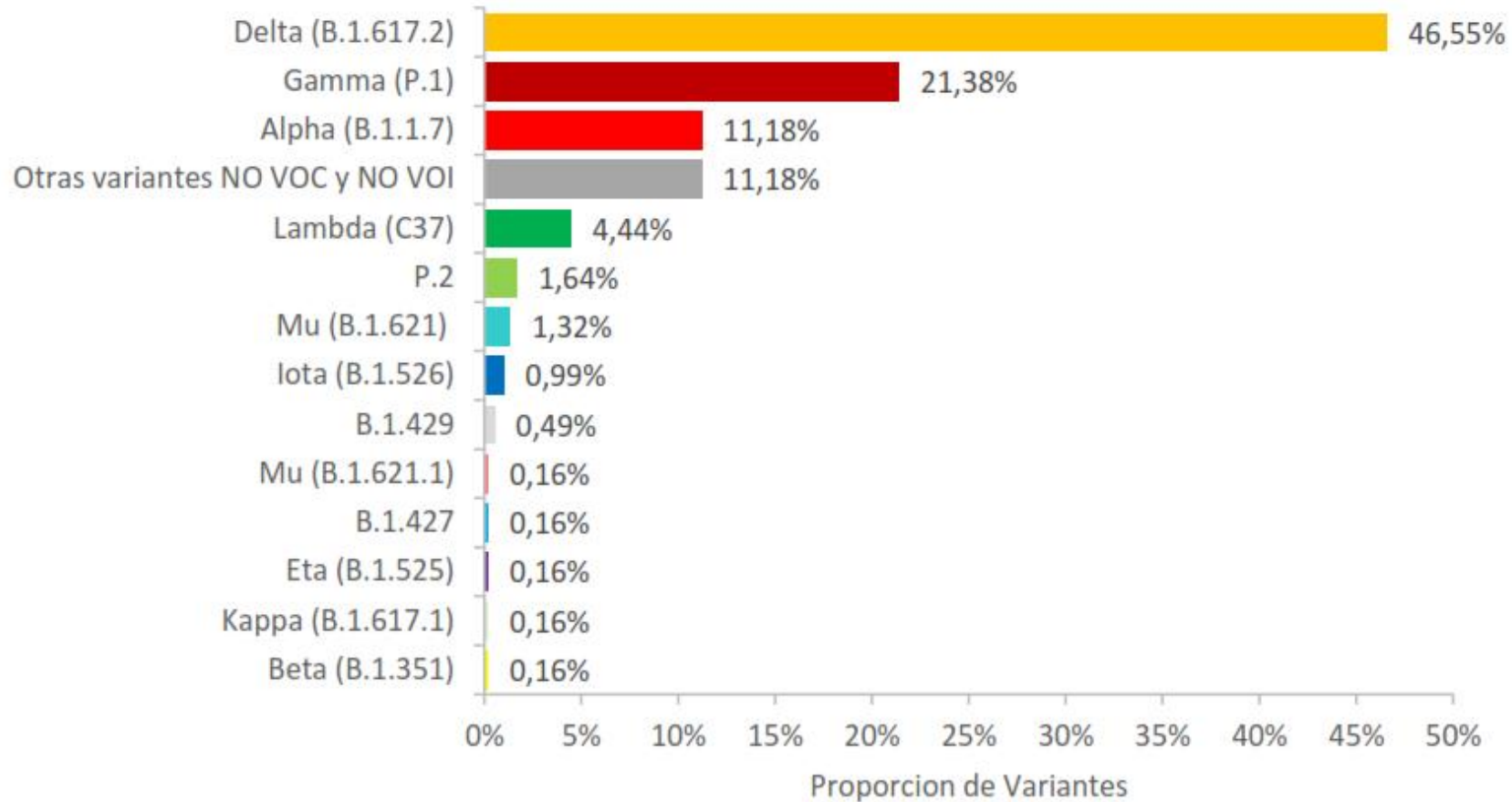
March 2021

1. circulation of the different SARS-CoV-2 variants in the community selecting representative samples
2. genetic characterisation to monitor the virus evolution
3. inform vaccine composition decisions or outbreak analyses

Whole Genome Sequencing
complete or partial S-gene
diagnostic screening PCR-based assays

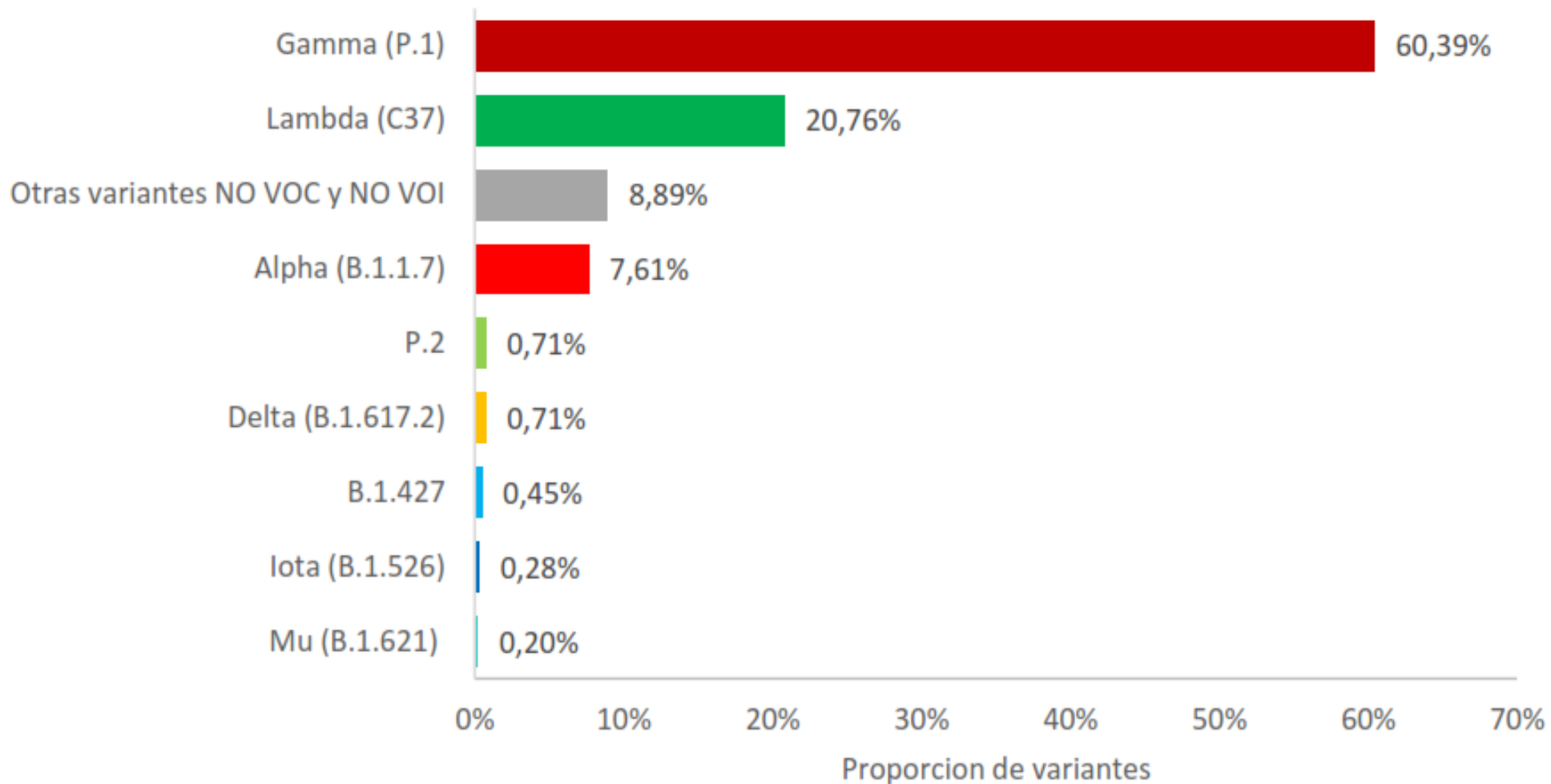
B.1.1.7/501Y.V1
B.1.351/501Y.V2
P.1/501Y.V3

Gráfico 1: Distribución porcentual de muestras correspondientes a variantes prioritarias y no prioritarias en viajeros y casos relacionados a la importación. n= 608



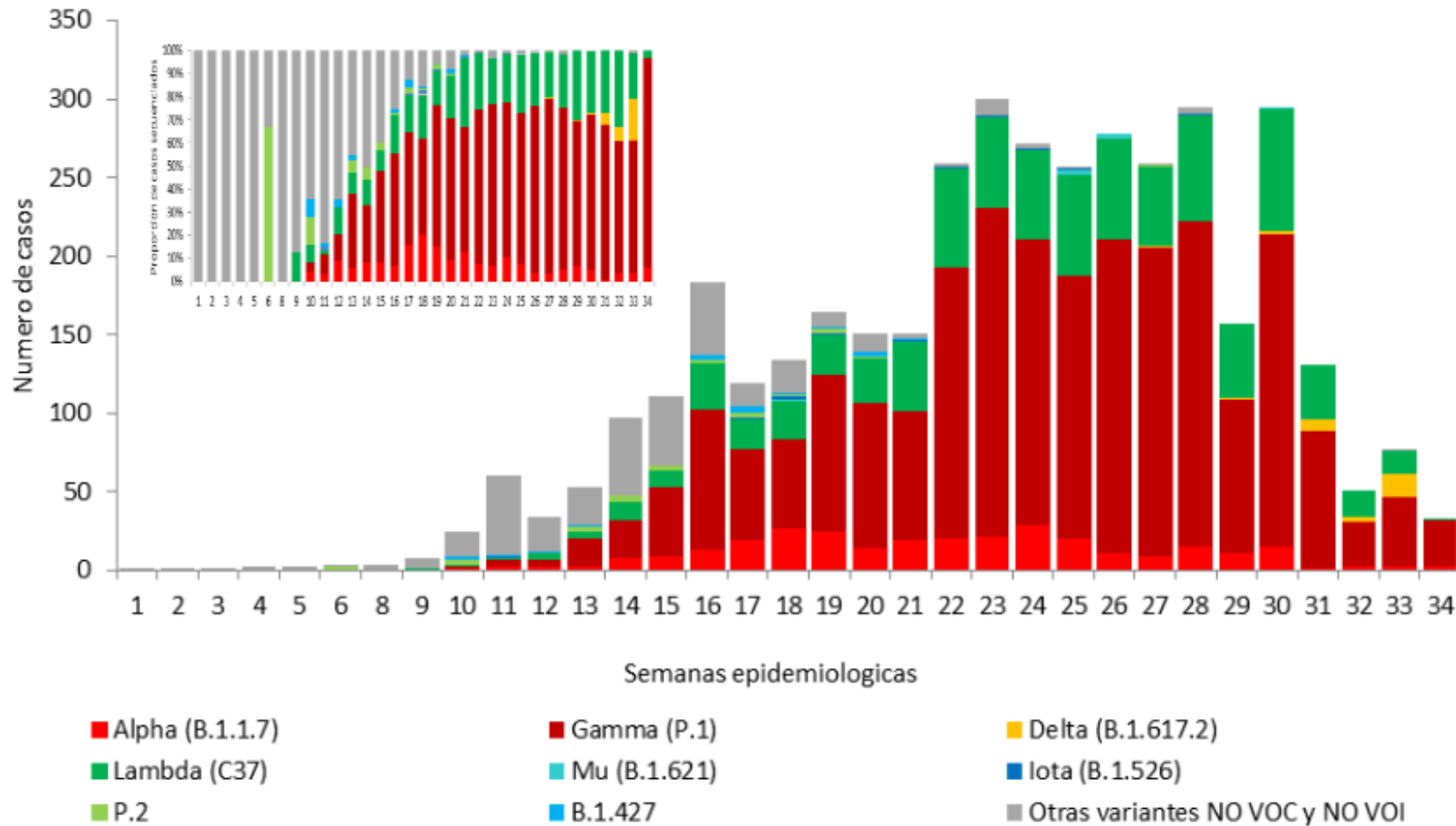
Fuente: Sistema Nacional de Vigilancia de la Salud (SNVS)

Gráfico 2: Distribución porcentual de muestras correspondientes a variantes prioritarias y no prioritarias en no viajeros. Total País. n= 3969



Fuente: Sistema Nacional de Vigilancia de la Salud (SNVS)

Gráfico 3: Distribución porcentual y absoluta de variantes identificadas en no viajeros según SE de toma de muestra. SE1- SE34. Total país.



Fuente: Sistema Nacional de Vigilancia de la Salud (SNVS)

Gráfico 4: Distribución relativa de muestras correspondientes a variantes prioritarias y no prioritarias en no viajeros por Región del País. Hasta la SE34. n= 3969

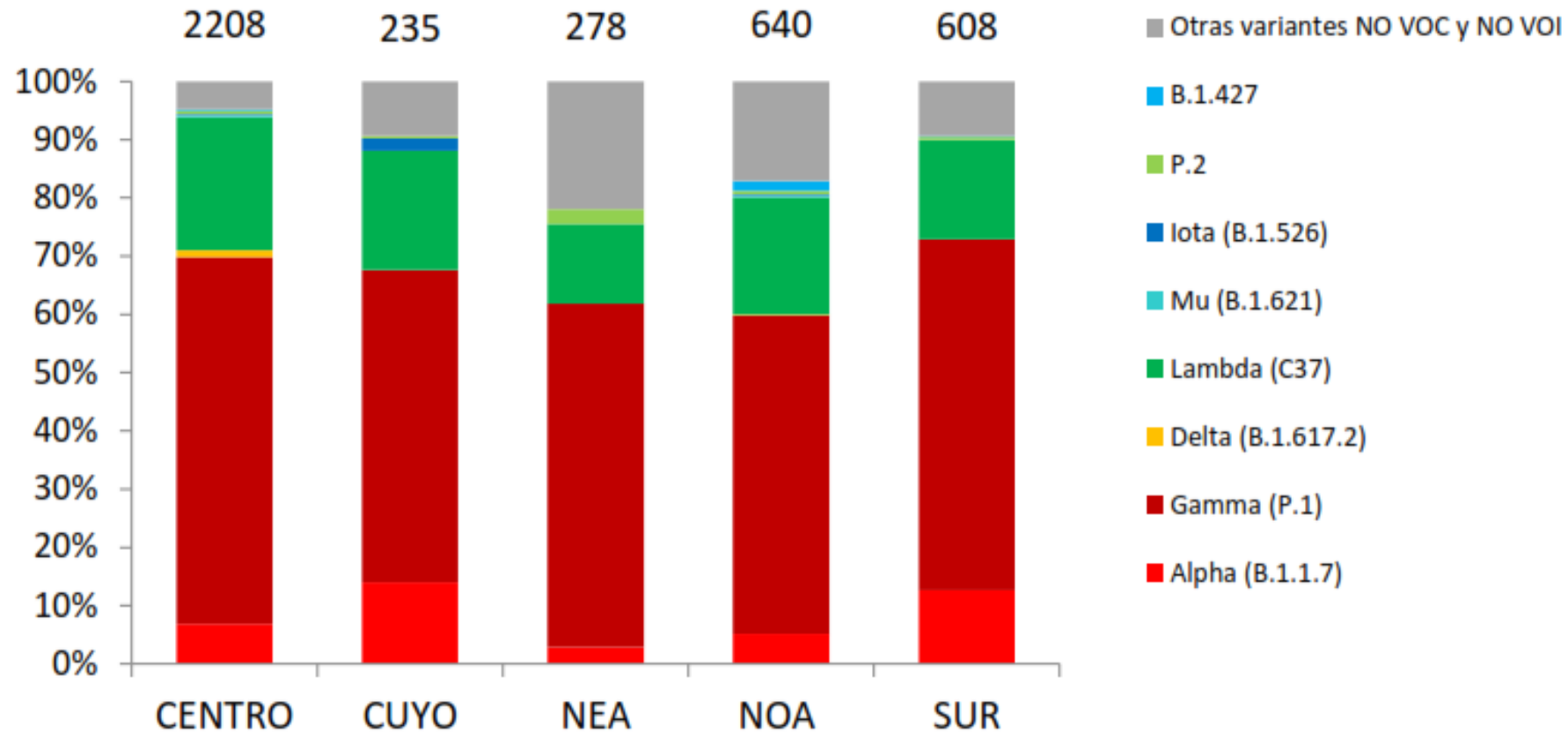
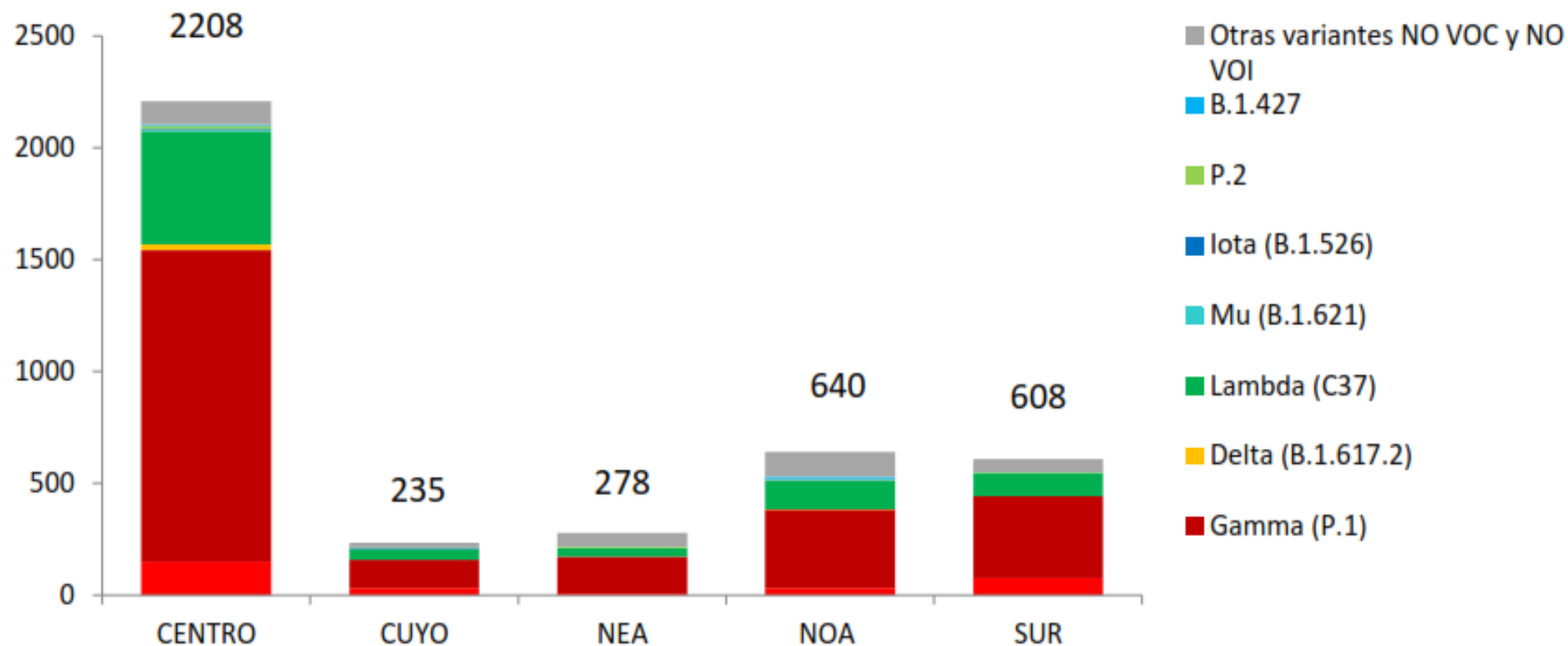


Gráfico 5: Distribución absoluta de muestras correspondientes a variantes prioritarias y no prioritarias en no viajeros por Región del País. Hasta la SE34. n= 3969



Fuente: Sistema Nacional de Vigilancia de la Salud (SNVS)

Grafico 6: Distribucion porcentual de muestras correspondientes a variantes Alpha (B.1.1.7), Gamma (P.1) y Lambda (C.37) en no viajeros por Región del País. Acumulados hasta la SE34.

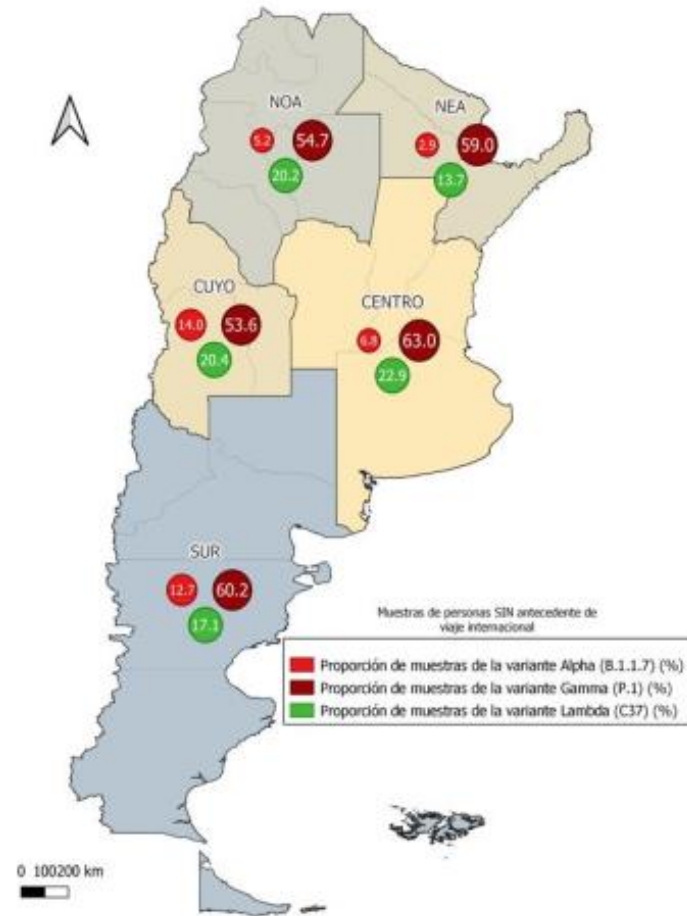
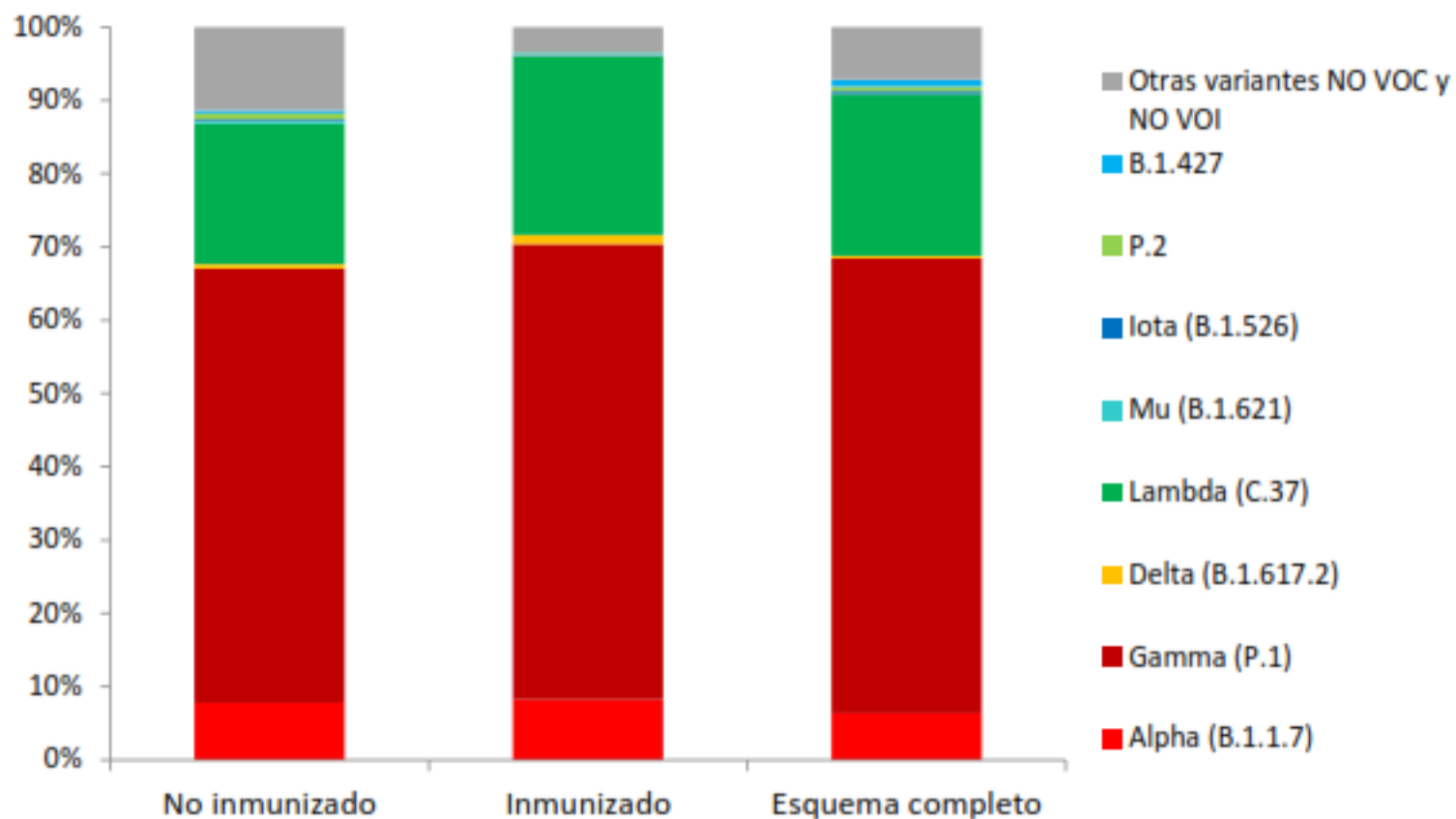


Gráfico 4: Distribución porcentual de variantes en casos secuenciados según condición de inmunización para el total país hasta SE34²⁸.



Fuente: Sistema Nacional de Vigilancia de la Salud (SNVS) y Registro Federal de Vacunación Nominalizado (NoMiVac)

SARS-CoV-2 Genetic Characterization

Final remarks:

- Mutations are naturally expected as part of the virus evolution and adaptation process.
- Although some have demonstrated enhanced capacity to replicate and transmit (particularly Delta), they are not necessarily more aggressive or lethal; the impact on re-infections or immune response escape is still to be established
- So far, there is no evidence to infer that current available vaccines do not work with these variants: significant decrease in severe cases, hospitalizations and death

SARS-CoV-2 Genetic Characterization

Final remarks:

- The more the virus is transmitted, the more the chance to generate mutations: More variants are expected to emerge (vaccine selection and evolution pressure)
- Preventing the transmission is the only way to avoid variants generation
- All the control and public health measures should be maintained (masks, social, distancing, isolation of cases, quarantine of contacts, vaccines...), regardless of the circulating variant

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Ezequiel Tuduri

**Red Nacional de Laboratorios de
influenzay otros virusa respiratorios**



Taller de la Red Nacional de
Laboratorios de influenza y
otros virus respiratorios .
Agosto 2019. INEI-ANLIS

Muchas gracias por su atención !!!!

