SÍRIO·LIBANÊS

SARS-CoV-2 Variants in Brazil

ISBT WP-TTID meeting
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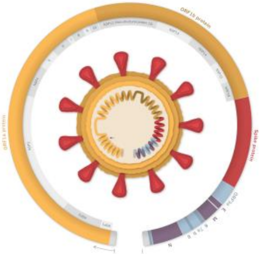


Acknowledgements: Edison Durigon and Rafael Machado
Virology Department – University of São Paulo

Variants of concern in Brazil – March, 2021

Disclaimer: This is not my main expertise field, so, don't push the questions too hard!!!

Main definitions (Racaniello):

- **Isolate: A virus that has been isolated from an infected host and propagated in culture (BetaCoV/Wuhan/WIV04/2019)**
- **Genome sequence: represents an isolate, *but is not an isolate!***
- **Variant: A virus whose genome sequence differs from that of a reference virus**
  - **There are several variants of concern (VOC) for SARS-CoV-2**
- **Strain: A variant that possesses unique and stable phenotypic characteristics, defined only by International Expert Group Committees (not journalists !)**
  - **There is, so far, only one SARS-CoV-2 strain!**
- **Serotype: Viruses of the same species that are antigenically distinct, usually defined by neutralization assays**
- **Genotype: A description of the genetic make-up of the virus**
- **Clade: A group of viruses composed of an ancestor and its descendants**
- **Lineage: Cluster of sequences associated with an epidemiological event (e.g. introduction of the virus into a distinct geographic area with evidence of onward spread).**

nextstrain.org

Variants of concern – NY Times - February 25, 2021

VARIANTS OF CONCERN - “THE TRIO INFERNALE”

Lineage	Variant name	Status
B.1.1.7	Variant of Concern 202012/01, or 501Y.V1	Emerged in Britain in December and is roughly 50 percent more infectious. Now detected in over 70 countries and 33 states.
B.1.351	501Y.V2	Emerged in South Africa in December. Reduces the effectiveness of some vaccines. **Not important in Brazil at this moment**
P.1	501Y.V3	Emerged in Brazil in late 2020. Has mutations similar to B.1.351.

Mutations that may help the coronavirus spread

Lineage	Mutation	Status
B.1	D614G	Appeared in early 2020 and spread around the world.
Several	N501Y	A defining mutation in several lineages, including B.1.1.7, B.1.351 and P.1. Helps the virus bind more tightly to human cells.
Several	E484K	Appears in several lineages. May help the virus avoid some kinds of antibodies.
Several	K417	Appears in several lineages, including B.1.351 and P.1. May help the virus bind more tightly to cells.
Several	L452R	Increasingly common in California, but not yet shown to be more infectious.
Several	Q677	Found in seven U.S. lineages, but not yet shown to be more infectious.

Other variants in the news

Lineage	Variant name	Status
B.1.427, B.1.429	CAL.20C	Common in California, but not yet shown to be more infectious. Carries the L452R mutation.
B.1.526	—	Spreading in New York. One version carries the E484K mutation, another carries S477N.

FEB 27TH 2021

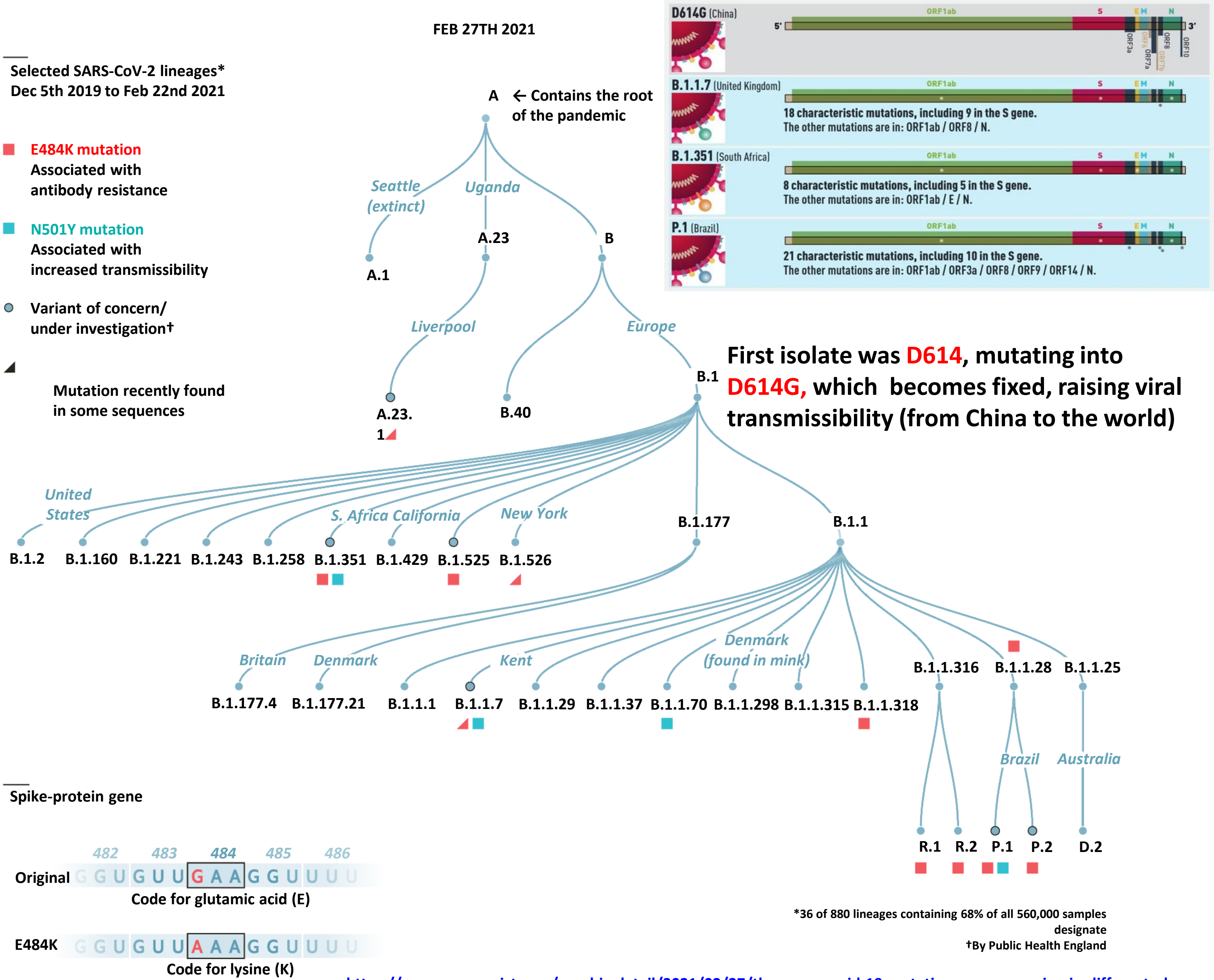
Selected SARS-CoV-2 lineages*
Dec 5th 2019 to Feb 22nd 2021

🟥 E484K mutation
Associated with
antibody resistance

🟦 N501Y mutation
Associated with
increased transmissibility

○ Variant of concern/
under investigation†

◢ Mutation recently found
in some sequences



18 characteristic mutations, including 9 in the S gene.
The other mutations are in: ORF1ab / ORF8 / N.

8 characteristic mutations, including 5 in the S gene.
The other mutations are in: ORF1ab / E / N.

21 characteristic mutations, including 10 in the S gene.
The other mutations are in: ORF1ab / ORF3a / ORF8 / ORF9 / ORF14 / N.

First isolate was D614, mutating into D614G, which becomes fixed, raising viral transmissibility (from China to the world)

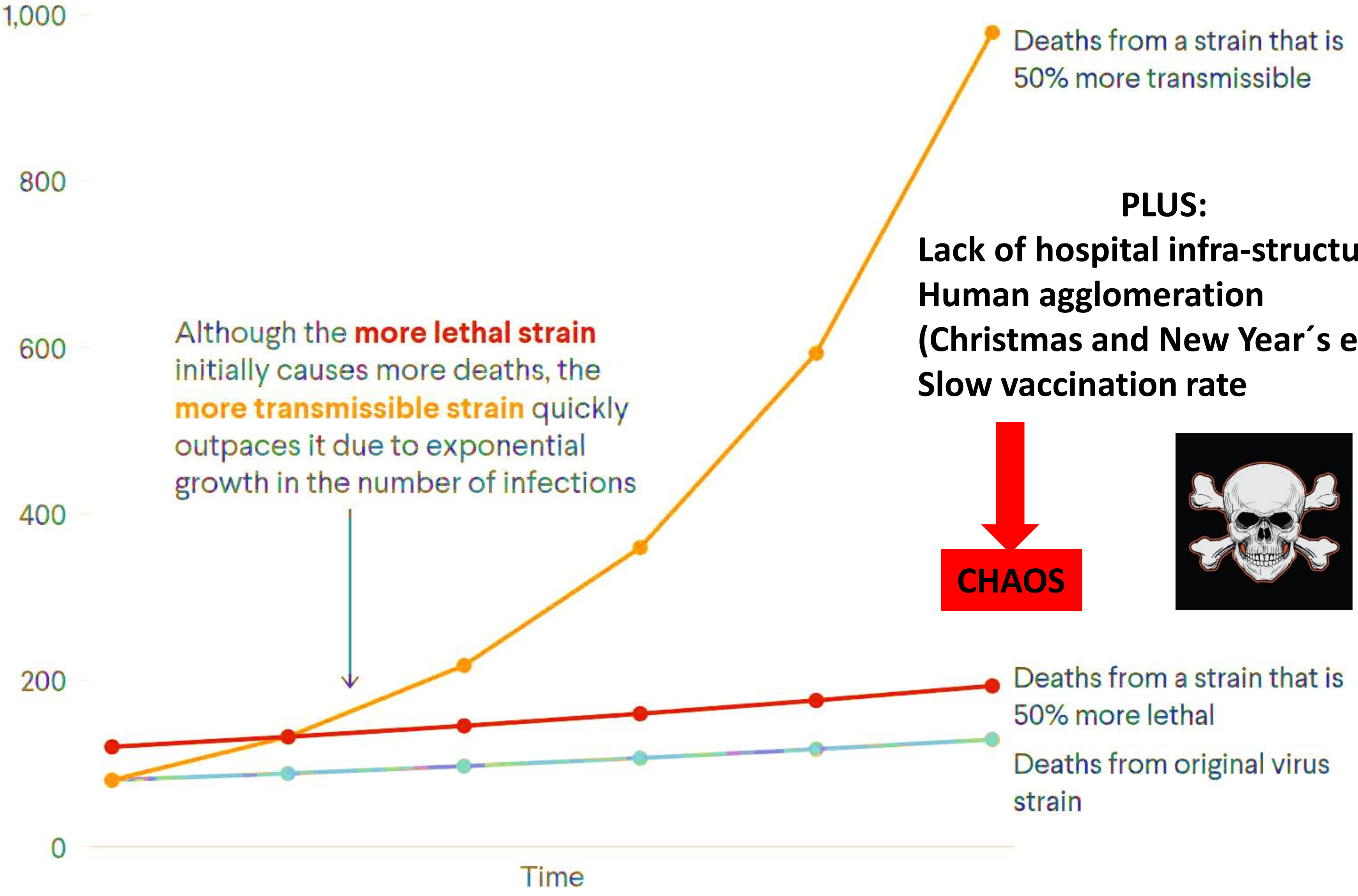
Spike-protein gene

Original G G U G U U G A A G G U U U U
Code for glutamic acid (E)

E484K G G U G U U A A A G G U U U U
Code for lysine (K)

*36 of 880 lineages containing 68% of all 560,000 samples designate
†By Public Health England

https://www.economist.com/graphic-detail/2021/02/27/the-same-covid-19-mutations-are-appearing-in-different-places



Although the **more lethal strain** initially causes more deaths, the **more transmissible strain** quickly outpaces it due to exponential growth in the number of infections

PLUS:

Lack of hospital infra-structure
Human agglomeration
(Christmas and New Year´s eve)
Slow vaccination rate

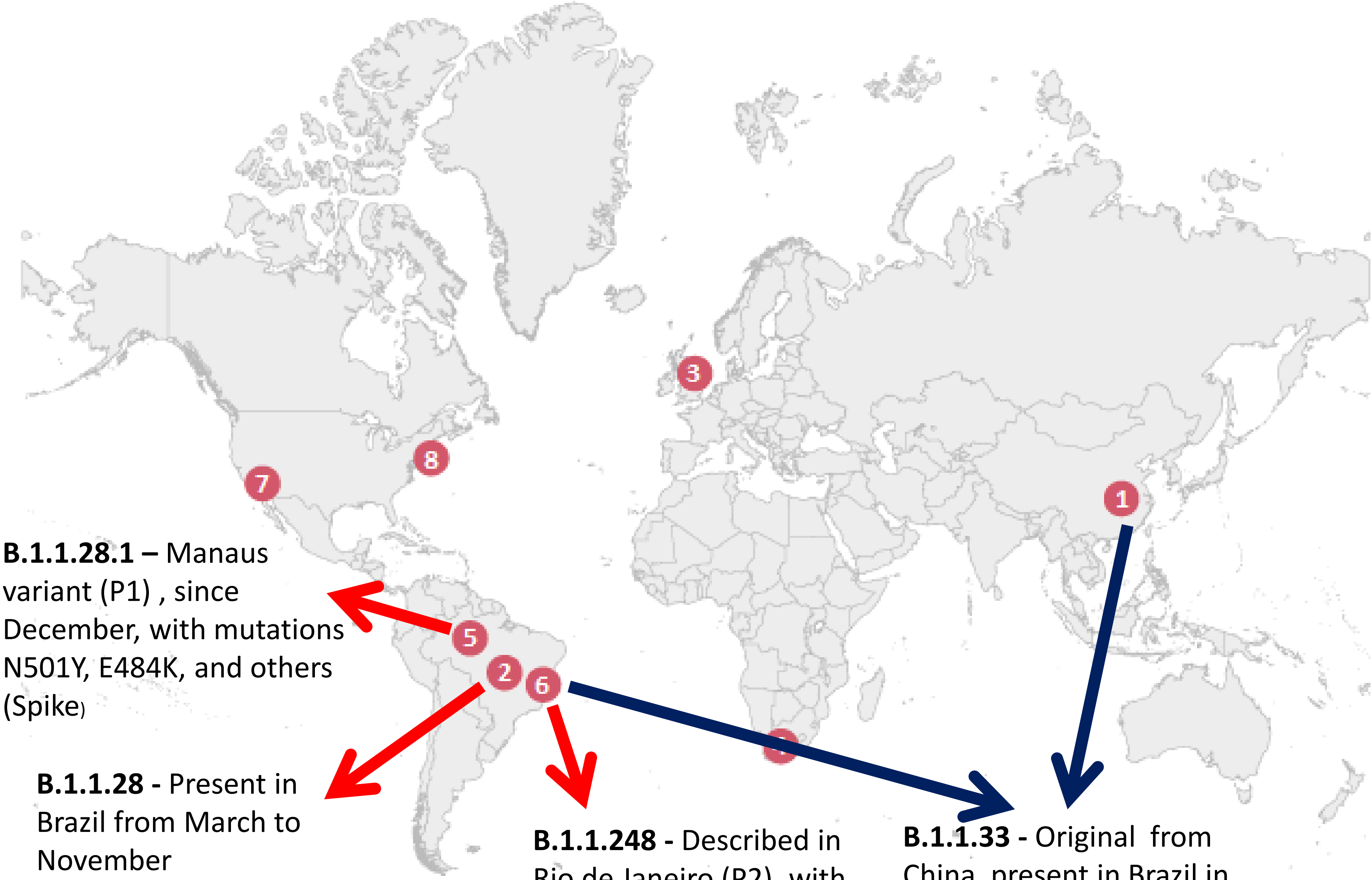
CHAOS

Notes: The line for the original strain assumes a fatality risk of 0.8% and that each infected person transmits the virus to 1.1 other people on average.

Source: Adam Kucharski, Associate Professor, London School of Hygiene and Tropical Medicine.

COUNCIL *on*
FOREIGN
RELATIONS

Variants of concern in Brazil – March, 2021



B.1.1.28.1 – Manaus variant (P1) , since December, with mutations N501Y, E484K, and others (Spike)

B.1.1.28 - Present in Brazil from March to November

B.1.1.248 - Described in Rio de Janeiro (P2), with mutation E484K (Spike)

B.1.1.33 - Original from China, present in Brazil in early stages of pandemia

Variants of concern in Brazil – March, 2021

Brazil

In January 2021, the P.1 variant was identified in 42% (13 out of 31) of RT-PCR positive samples collected between 15 and 23 December in Manaus, Amazonia, Brazil (Faria 2021). At the time, Manaus was experiencing an upsurge in COVID-19 cases. P.1 has 10 mutations in the spike protein (Faria 2021) and some, including N501Y and E484K, have been reported in B.1.1.7 and B.1.351, the variants first detected in the UK and South Africa.

Also identified in travellers arriving in Japan from Brazil

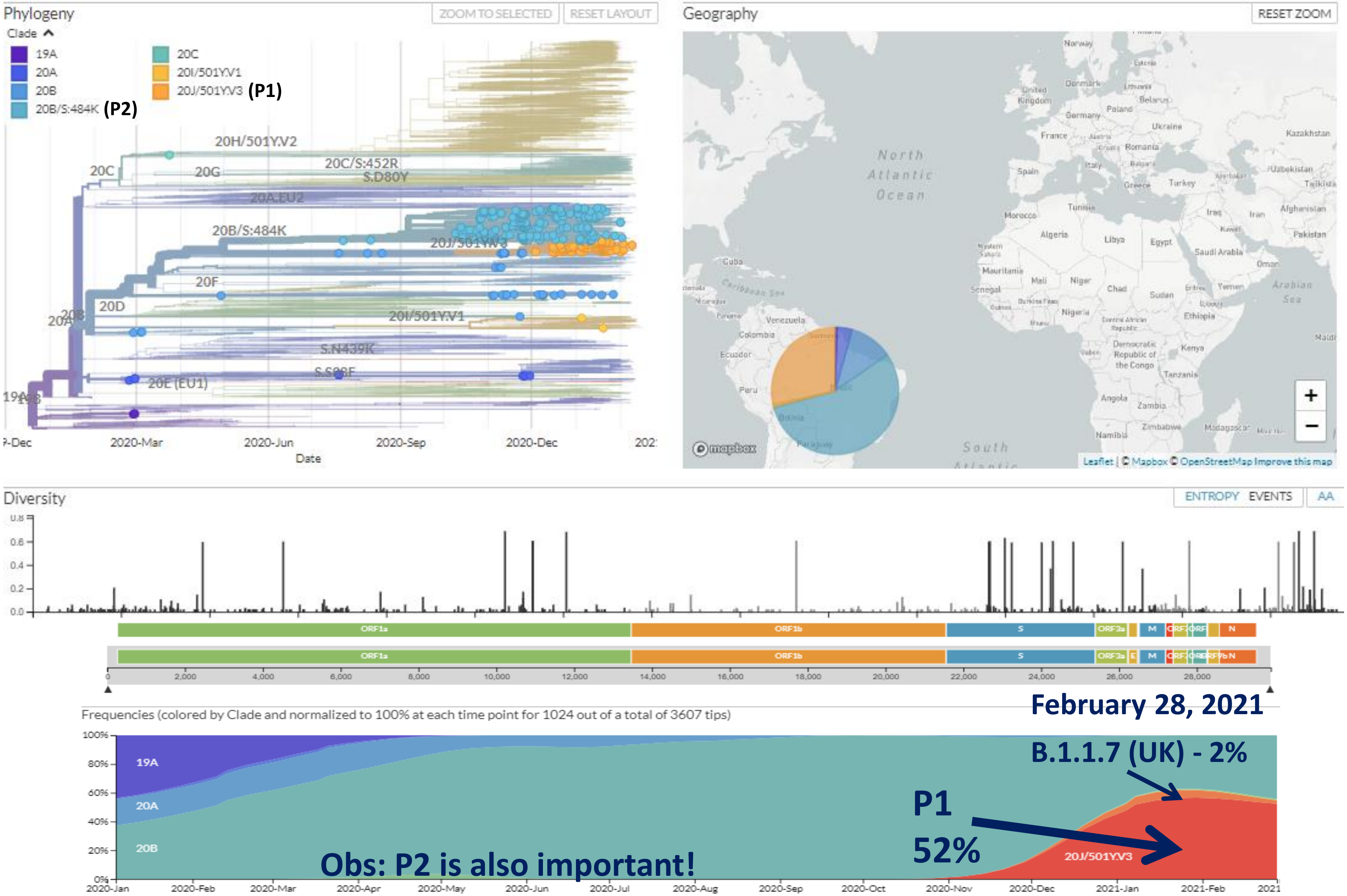
Associated with multiple mutations in Spike, including: SN501Y, E484K, K417N and SH655Y.

Also, a mutation in Nucleocapsid: P80R and the deletion in ORF1a at positions 3675-3677 (also in 501Y.V1 and 501Y.V2).

https://covidreference.com/Variants

Variants of concern in Brazil – March, 2021

https://nextstrain.org/ncov/south-america?f_country=Brazil&r=region



(P2)

(P1)

February 28, 2021

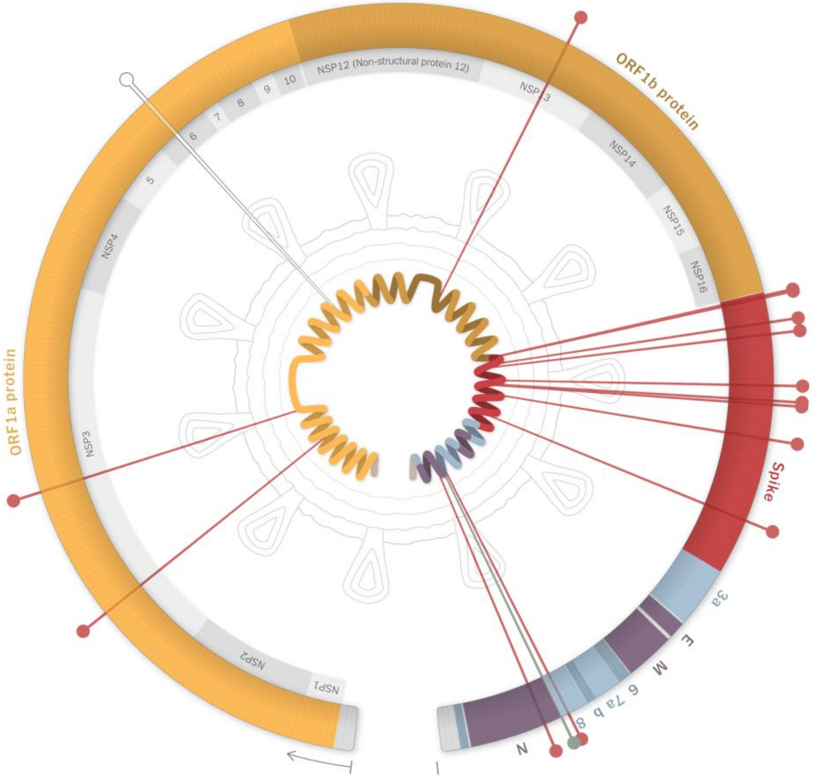
B.1.1.7 (UK) - 2%

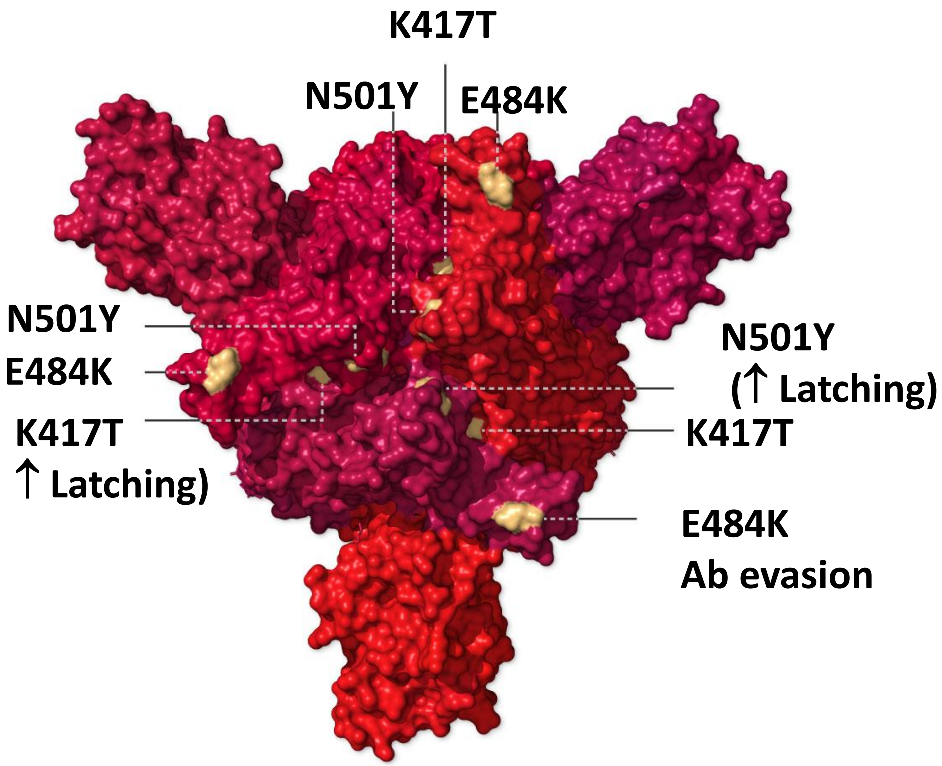
P1

52%

Obs: P2 is also important!

MUTATION 20J/501Y.V3 – P1 Spike (Offshoot B.1.1.28.1)





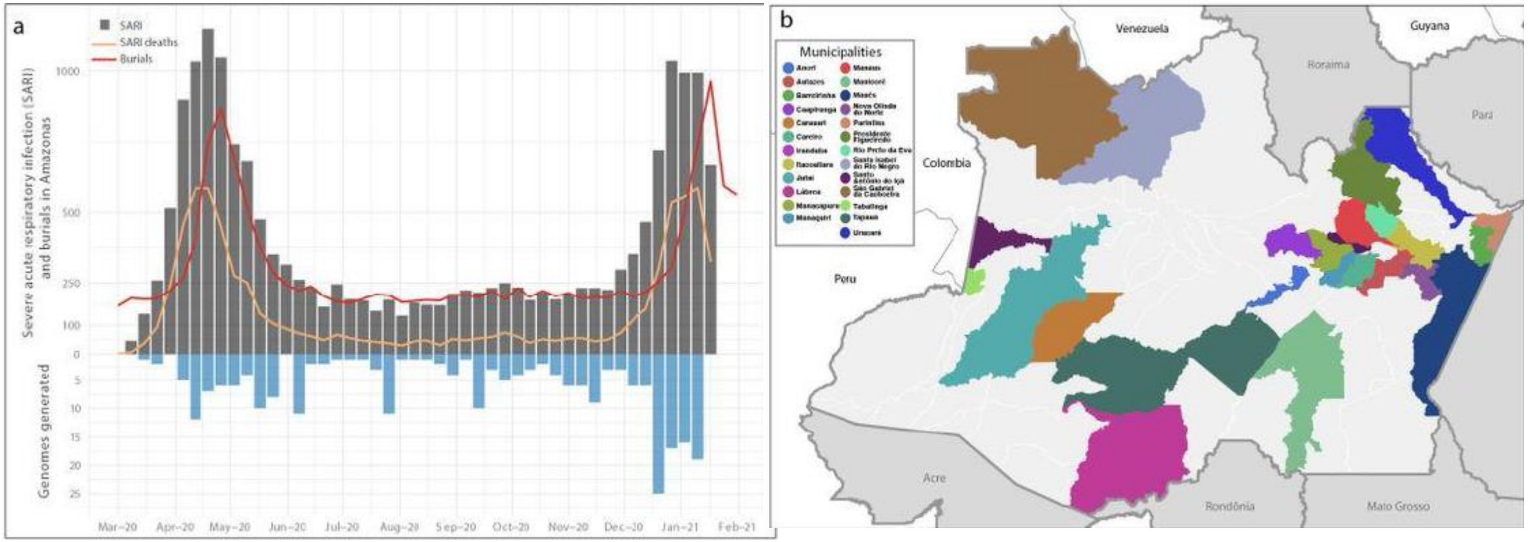
- First discovered in Japan (Dec 20) from 4 travellers to Manaus
- Described 4 days later in Manaus , descendant of B.1.1.28 (Faria et al)
- Predominant lineage in northern Brazil
- Close relative of B.1.351 lineage (South Africa)
- Several mutations

Amazon lineages – update February, 2021

Time period	P.1	P.2	B.1.1.28	Others	Total
November 2020	0	1 (4%)	19 (79%)	4 (17%)	24
December 2020	28 (51%)	6 (11%)	17 (31%)	4 (7%)	55
January 2021	32 (91%)	2 (6%)	0	1 (3%)	35

Table. Temporal distribution of SARS-CoV-2 lineages in the Amazonas state

*** 7 weeks from 0 to 87%**



Amazon State: 4.2 million people - Area: 1.571 million km^2

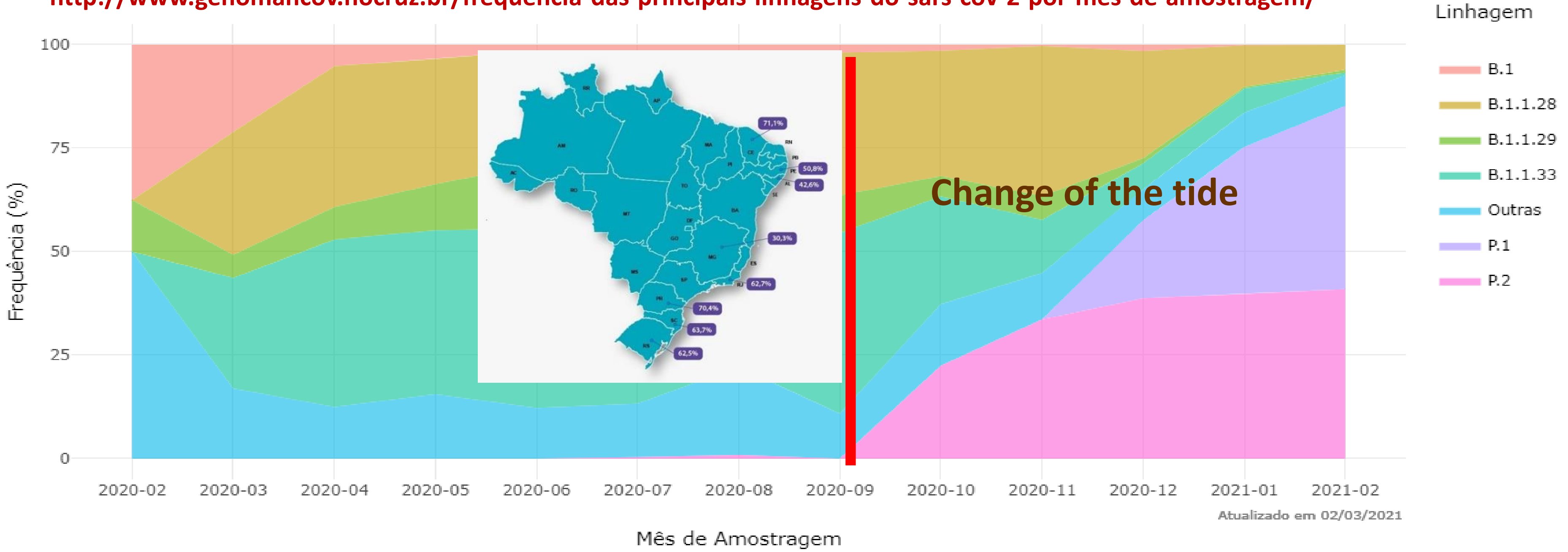
"Our results also point that the P.1 lineage emerged in a short time frame and disseminated fast outside Manaus reaching nearby municipalities of the Metropolitan region as well as very distant municipalities located at the border region with neighbouring South American countries."

It seems that social distancing wasn´t quite well respected in the Amazon State

https://virological.org/t/phylogenetic-relationship-of-sars-cov-2-sequences-from-amazonas-with-emerging-brazilian-variants-harboring-mutations-e484k-and-n501y-in-the-spike-protein/585/2

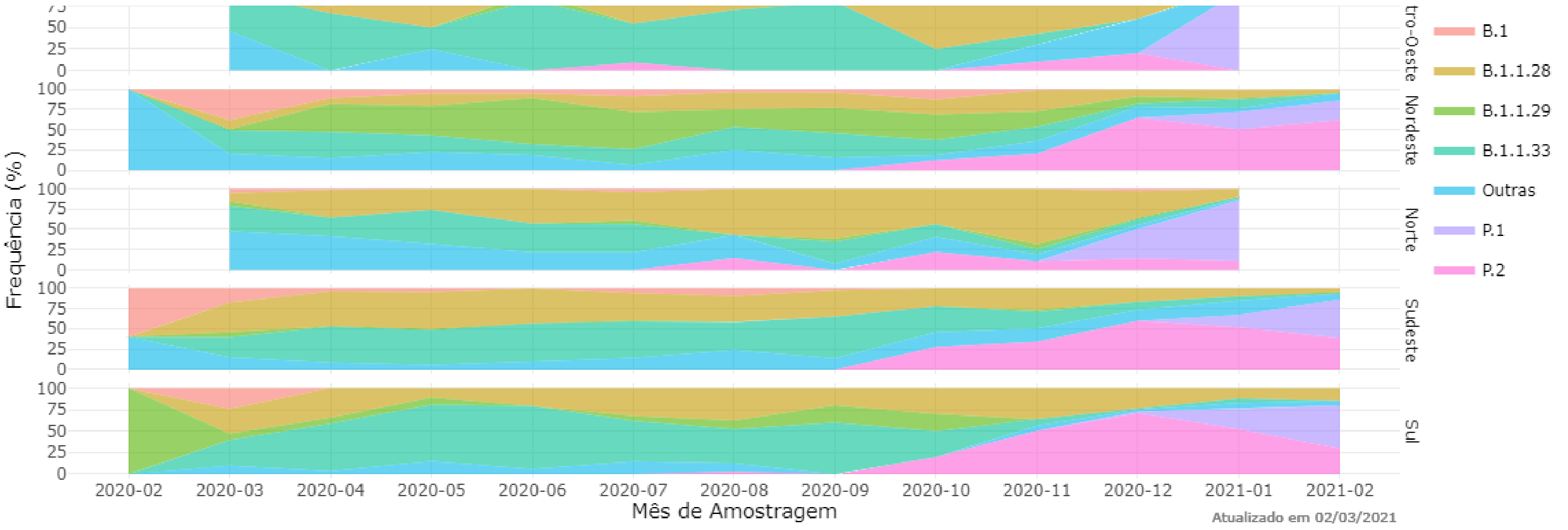
Variants of concern in Brazil – March, 2021

http://www.genomahcov.fiocruz.br/frequencia-das-principais-linhagens-do-sars-cov-2-por-mes-de-amostragem/



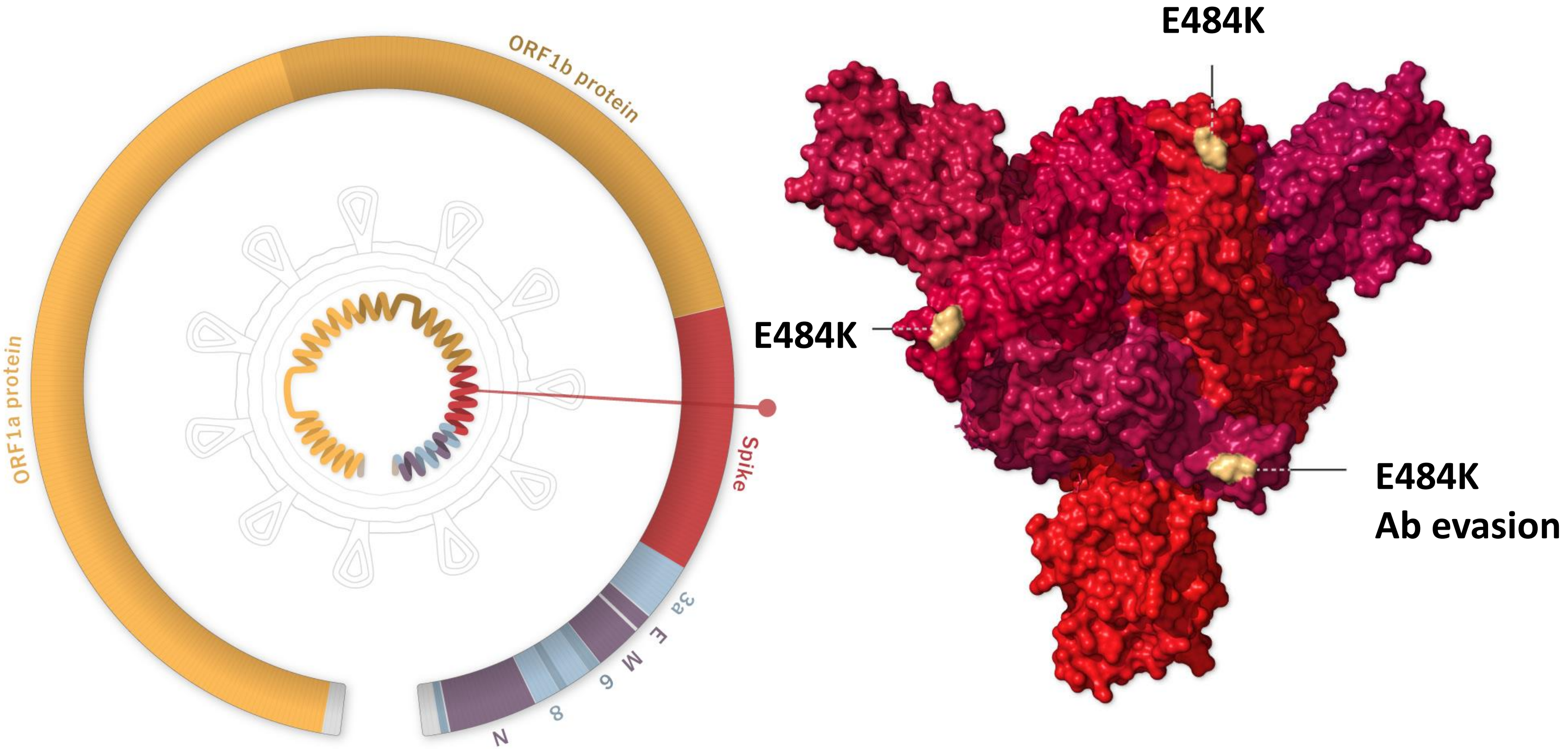
Change of the tide

Atualizado em 02/03/2021



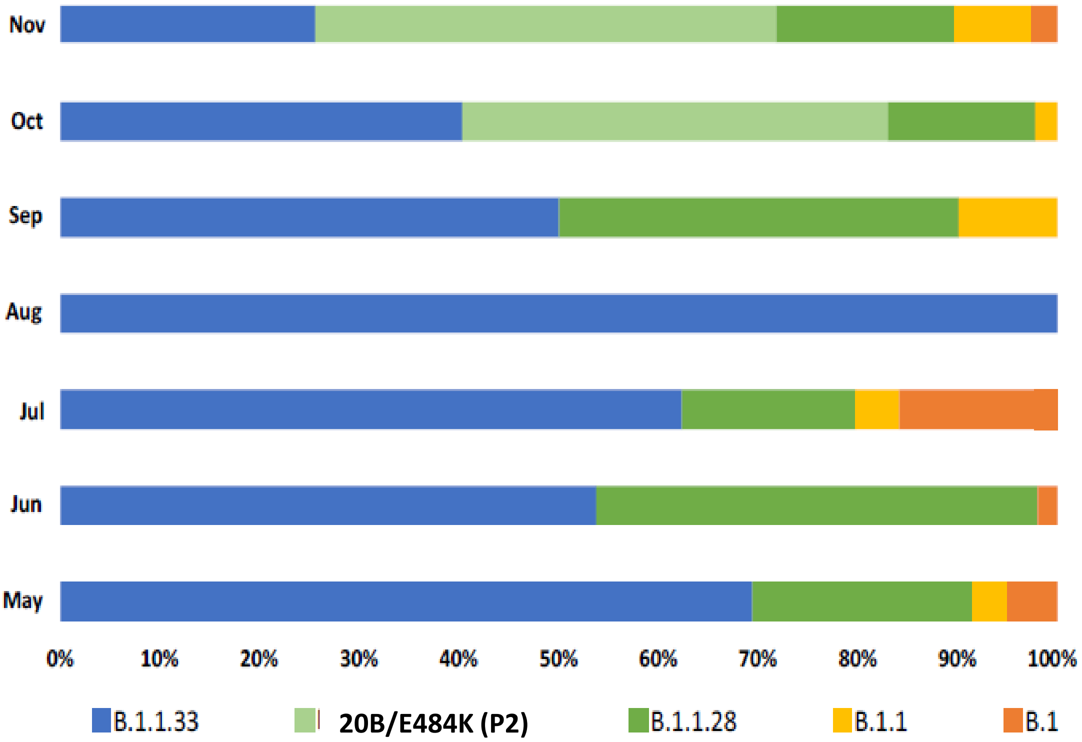
Atualizado em 02/03/2021

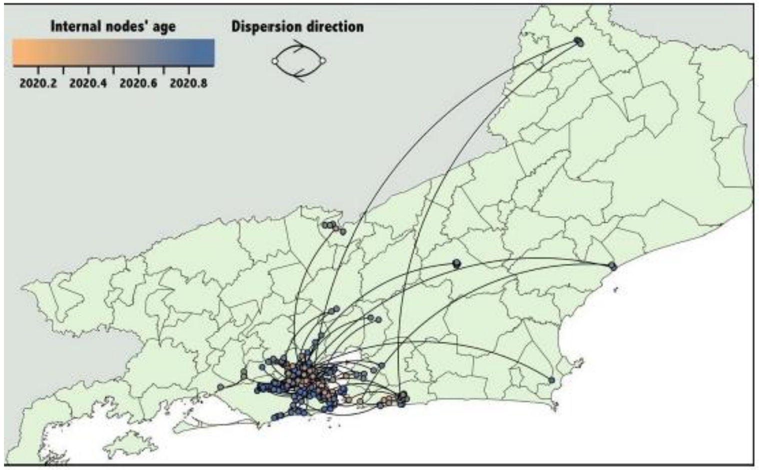
MUTATION B.1.1.248 E484K – Spike P2



- Near the top of spike, altering the shape of protein (↑ infectious)
- Described in Rio de Janeiro (January, Voloch et al.)
- Spread to south (PR, RS), North /Norheast (AL, PB and AM)
- Arrived in São Paulo
  - December - <1%
  - March – Majority of sequenced samples

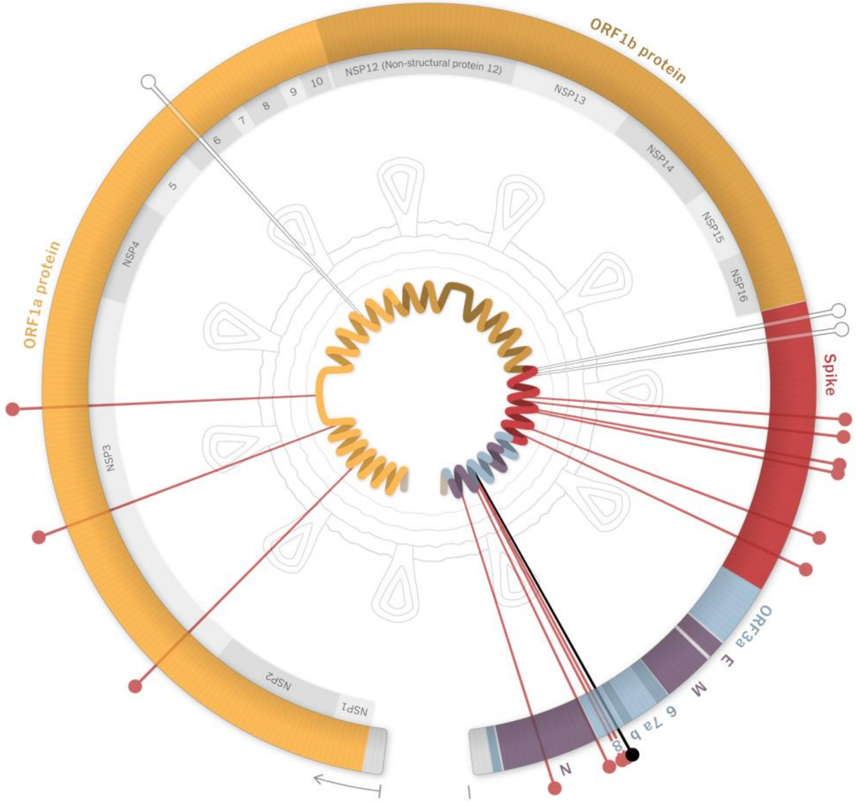
Variants of concern in Brazil – March, 2021
P2 Mutant

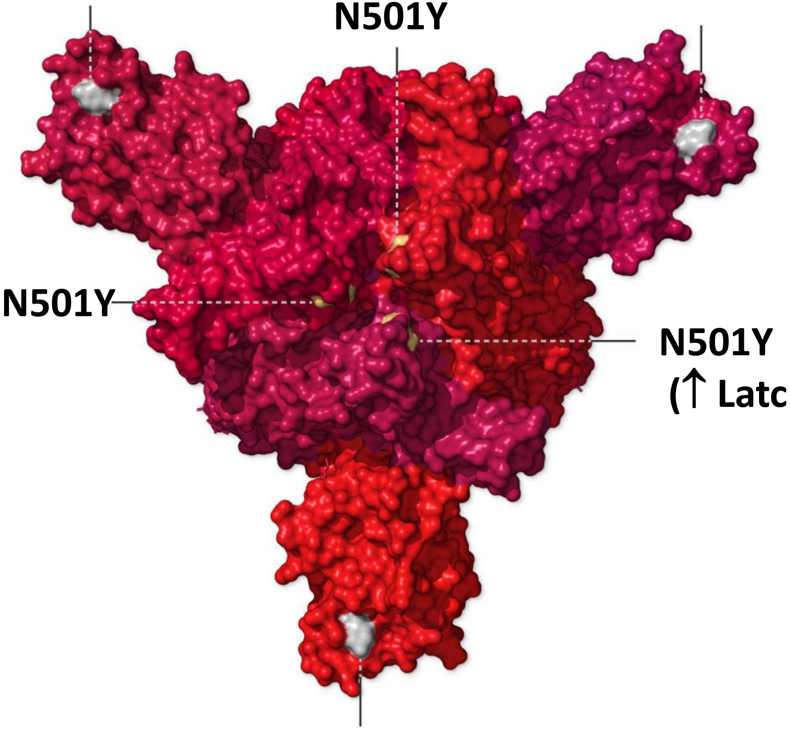




Evolution of relative frequency of 180 Brazilian SARS-CoV-2 lineages (Voloch *et al*. J Virol 2021. DOI: 10.1128/JVI.00119-21)

MUTATION 20I/501Y.V1 - B.1.1.7 Spike





Y144/145

Y144/145

N501Y

N501Y

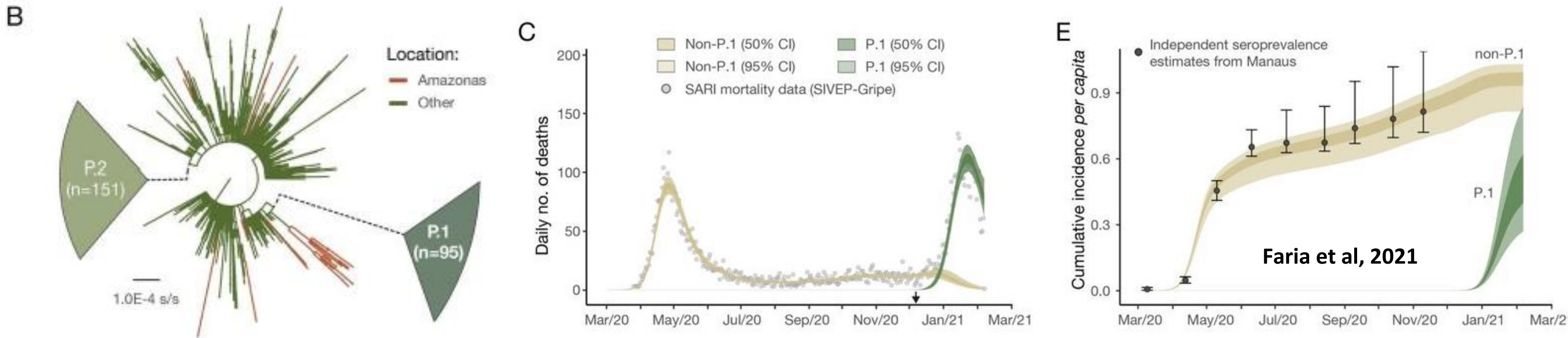
N501Y
(↑ Latching)

Y144/145
(Ab evasion?)

30-50% more infectious, and possibly, 35% more deadly than other strains

Variants of concern in Brazil – March, 2021

* E484 – Probably, the most important site for Ab (mono/poly) evasion	**P1 (Brazil)** November 20 1 mo before upsurge	**P2 (Brazil)** Jul ?/ Oct 20	**B.1.1.7 (UK)** September 20
Other names	**N501.V3**	**484K.V2**	**N501.V1**
Mutations	**21**	**5**	**23**
Spike mutations	**10 (E484K*,N501Y)**	**E484K***	**8 (N501Y)**
Immune escape (MoAb)	**Likely (REGN10989/LYCov555)**	**Likely**	**Partial/unlikely (Class 1 MoAb)**
Reinfection	**Yes**	**Yes**	**No**
Herd Immunity	**Manaus-76%** **Donors are not a good example**	**?**	**?**
Cellular immunity CD4+/CD8+ (Tarke)	**Preserved** **(>90% epitopes conserved)**	**Unknown**	**Preserved** **(>90% epitopes conserved)**
Vaccine (AZ/Cvac)	**+/+ (↓ Pfizer)**	**?/+**	**+/+**
Affected countries	**24**	**8**	**82**



Faria et al, 2021

Variants of concern in Brazil – March, 2021

Final Conclusion:

Whoever claims to have the final word on any aspect of SARS-CoV-2 is either a lunatic or genius, however...

There are more lunatics than geniuses in the world....