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Variants vaccine safety/efficacy. An update as to the epidemiology of P1, and/or effects of the currently available vaccines on the P1 variant

Marcos da Silva Freire, DSc.





#### ARTICLE

COVID-19 epidemic in the Brazilian state of Amazonas was driven by long-term persistence of endemic SARS-CoV-2 lineages and the recent emergence of the new Variant of Concern P.1

Felipe Naveca, Valdinete Nascimento, Victor Souza, André Corado, Fernanda Nascimento, George Silva, Ágatha Costa, Débora Duarte, Karina Pessoa, Matilde Mejía, Maria Brandão, Michele Jesus, Luciana Gonçalves, Cristiano da Costa, Vanderson Sampaio, Daniel Barros, Marineide Silva, Tirza Mattos, Gemilson Pontes, Ligia Abdalla, João Santos, Ighor Arantes, Filipe Dezordi, Marilda Siqueira, Gabriel Wallau, Paola Resende, Edson Delatorre, Tiago Gräff, Gonzalo Bello

DOI: 10.21203/rs.3.rs-275494/v1 🚦 Download PDF

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HEALTHCARE & PHARMACEUTICALS JANUARY 10, 2021 S:14 AM / UPDATED 2 MONTHS AGO

## Japan finds new coronavirus variant in travellers from Brazil



2 MIN READ 🕴 🕊



#### Novel SARS-CoV-2 Variant in Travelers from Brazil to Japan

Takahisa Fujino, Hidetoshi Nomoto, Satoshi Kutsuna, Mugen Ujiie, Tetsuya Suzuki, Rubuna Sato, Tsuguto Fujimoto, Makoto Kuroda, Takaji Wakita, Norio Ohmagari

Author affiliations: National Center for Global Health and Medicine, Tokyo, Japan (T. Fujino, H. Nomoto, S. Kutsuna, M. Ujile, T. Suzuki, R. Sato, N. Ohmagari); Tohoku University, Miyagi, Japan (H. Nomoto, T. Suzuki, N. Ohmagari); National Institute of Infectious Diseases, Tokyo (T. Fujimoto, M. Kuroda, T. Wakita)

#### DOI: https://doi.org/10.3201/eid2704.210138

Multiple severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants with higher transmission potential have been emerging globally, including SARS-CoV-2 variants from the United Kingdom and South Africa. We report 4 travelers from Brazil to Japan in January 2021 infected with a novel SARS-CoV-2 variant with an additional set of mutations.

Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 27, No. 4, April 2021



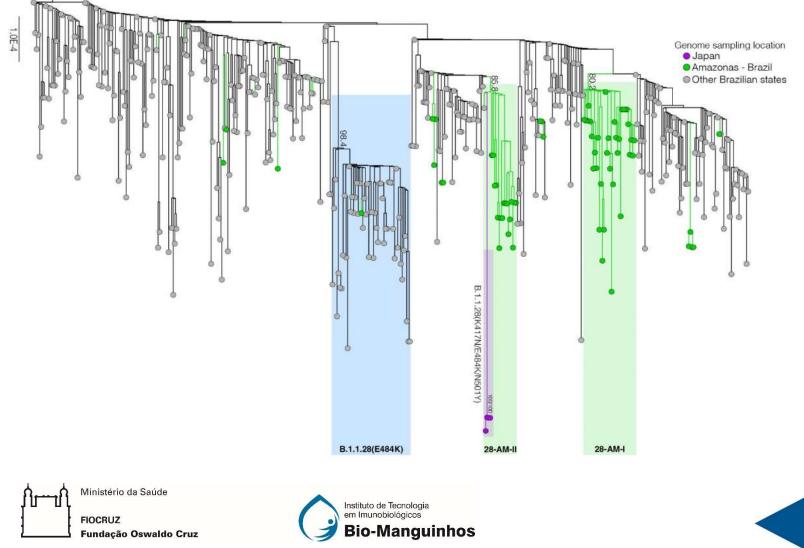
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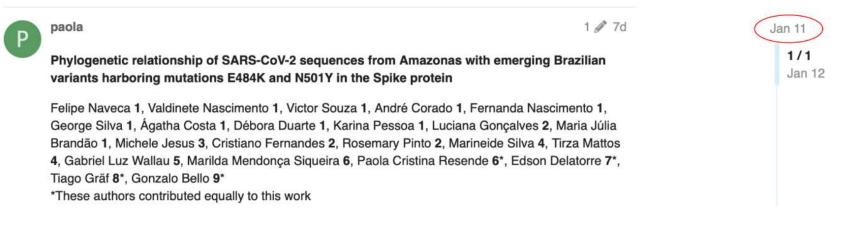


## B.1.1.28 Amazonas and Japan



### Phylogenetic relationship of SARS-CoV-2 sequences from Amazonas with emerging Brazilian variants harboring mutations E484K and N501Y in the Spike protein

SARS-CoV-2 coronavirus nCoV-2019 Genomic Epidemiology



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



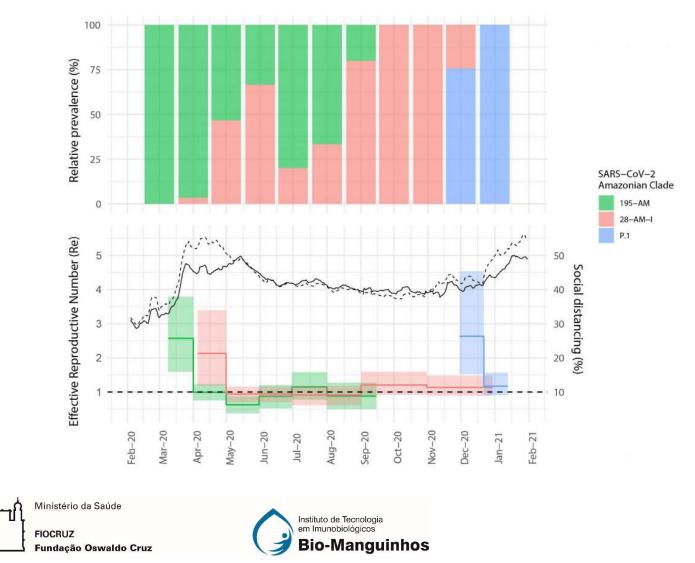
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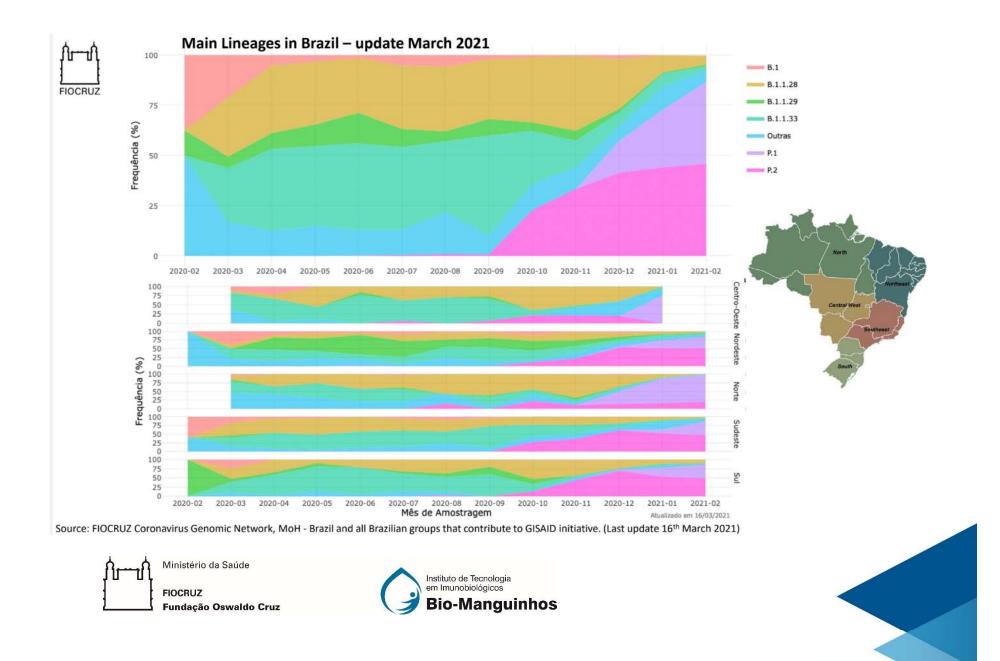




## Amazonian







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#### RESEARCH ARTICLE

## Three SARS-CoV-2 reinfection cases by the new Variant of Concern (VOC) P.1/501Y.V3

Felipe Naveca, Cristiano da Costa, Valdinete Nascimento, Victor Souza, André Corado, Fernanda Nascimento, Ágatha Costa, Débora Duarte, George Silva, Matilde Mejía, Karina Pessoa, Luciana Gonçalves, Maria Júlia Brandão, Michele Jesus, Marineide Silva, Tirza Mattos, Lígia Abdalla, João Hugo Santos, Rubens Costa-Filho, Tsuyoshi Sekizuka, Kentaro Itokawa, Masanori Hashino, Makoto Kuroda, Marilda Mendonça Siqueira, Gabriel Luz Wallau, Edson Delatorre, Tiago Gräf, Gonzalo Bello, Paola Cristina Resende

#### DOI: 10.21203/rs.3.rs-318392/v1 🚺 Download PDF

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#### Communication

#### A potential SARS-CoV-2 variant of interest (VOI) harboring mutation E484K in the Spike protein was identified within lineage B.1.1.33 circulating in Brazil

Paola Cristina Resende 1\*; Tiago Gräf 2\*#; Anna Carolina Dias Paixão 1; Luciana Appolinario 1; Renata Serrano Lopes 1; Ana Carolina da Fonseca Mendonça 1; Alice Sampaio Barreto da Rocha 1; Fernando Couto Motta 1; Lidio Gonçalves Lima Neto 3; Ricardo Khouri 2,4; Camila Indiani de Oliveira 2,4; Pedro Santos-Muccillo 2,5; João Felipe Bezerra 6; Dalane Loudal Florentino Teixeira 7; Irina Riediger 8; Maria do Carmo Debur 8; Rodrigo Ribeiro-Rodrigues 9; Anderson Brandao Leite 10; Cliomar Alves do Santos 11; Tatiana Schäffer Gregianini 12; Sandra Bianchini Fernandes 13; André Felipe Leal Bernardes 14; Andrea Cony Cavalcanti 15; Fábio Miyajima 16; Claudio Sachhi 17; Tirza Mattos 18; Cristiano Fernandes da Costa 19; Edson Delatorre 20\*\*; Gabriel L Wallau 21\*\*; Felipe G Naveca 22\*\*; Gonzalo Bello 23\*\*; Marilda Mendonça Siqueira 1\*\* on behalf of Fiocruz COVID-19 Genomic Surveillance Network

#### N.9

Genomic region (protein)	Nucleotide	Amino acid		
ORF1a	G1264T	-		
ORF1a	C7600T	-		
ORF1a (NSP3)	C7851T	A2529V (A1711V)		
ORF1a (NSP6)	T11078C	F3605L (F36L)		
Spike (S)	G23012A	——> E484K		
ORF7b (NSP7b)	A27853C	E33A		

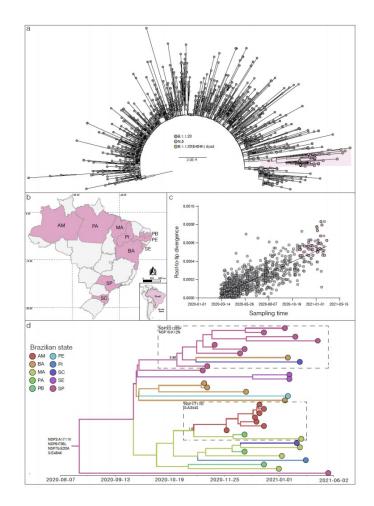
#### Now accepted for publication in Viruses

Table 1. Synapomorphic mutations of SARS-CoV-2 lineage N.9.





MDPI





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#### The ongoing evolution of variants of concern and interest of SARS-CoV-2 in Brazil revealed by convergent indels in the amino (N)terminal domain of the Spike protein

Paola Cristina Resende, Felipe G Naveca, Roberto D. Lins, Filipe Zimmer Dezordi, Matheus V. F. Ferraz, Emerson G. Moreira, Danilo F. Coêlho, Fernando Couto Motta, Anna Carolina Dias Paixão, Luciana Appolinario, Renata Serrano Lopes, Ana Carolina da Fonseca Mendonça, Alice Sampaio Barreto da Rocha, Valdinete Nascimento, Victor Souza, George Silva, Fernanda Nascimento, Lidio Gonçalves Lima Neto, Irina Riediger, Maria do Carmo Debur, Anderson Brandao Leite, Tirza Mattos, Cristiano Fernandes da Costa, Felicidade Mota Pereira, Ricardo Khouri, André Felipe Leal Bernardes, Edson Delatorre, Tiago Gräf, Marilda Mendonça Siqueira, Gonzalo Bello, D Gabriel L Wallau

#### Table 1. SARS-CoV-2 Brazilian variants with indels at NTD of the Spike protein.

Sample(s)	Lineage	NTD Indel	RBD	GISAID ID	
AM-FIOCRUZ-20842572LS/2020*	B.1.1.28	Δ144	-	EPI_ISL_1068132	
MG-FIOCRUZ-8180/2021	P.2	$\Delta 144$	E484K	EPI_ISL_1219137	
BA53/2021* BA54/2021* BA55/2021* BA-FIOCRUZ-7029/2021*	P.1	Δ144	K417T E484K N501Y	EPI_ISL_1067729 EPI_ISL_1067733 EPI_ISL_1067734 EPI_ISL_1219136	
AL-FIOCRUZ-4795/2021* PR-FIOCRUZ-5273/2021**	P.1	Δ141-144	K417T E484K N501Y	EPI_ISL_1219134 EPI_ISL_1219133	
AL-FIOCRUZ-4786/2021*	P.1	Δ189-190	K417T E484K N501Y	EPI_ISL_1219135	
MA-FIOCRUZ-6871/2021 MA-FIOCRUZ-6874/2021	B.1.1.33 (E484K)	Δ141-144 Δ211 Δ256-258	V445A E484K	EPI_ISL_1181371 EPI_ISL_1181370	
AM-FIOCRUZ-208972690P* AM-FIOCRUZ-20897281WS* AM-FIOCRUZ-21840593CL* PR-FIOCRUZ-5241/2021	B.1.1.28 (P.1-like)	ins214ANRN	K417T E484K N501Y	EPI_ISL_1068256 EPI_ISL_1219132 EPI_ISL_1261122 EPI_ISL_1261123	

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#### Cell

#### ARTICLE | ONLINE NOW

#### Antibody evasion by the P.1 strain of SARS-CoV-2

Wanwisa Dejnirattisai \* Daming Zhou \* Piyada Supasa \* Chang Liu \* Alexander J. Mentzer \* Helen M. Ginn • Yuguang Zhao • Helen M.E. Duyvesteyn • Aekkachai Tuekprakhon • Rungtiwa Nutalai • Beibei Wang • Guido C. Paesen • César López-Camacho • Jose Slon-Campos • Thomas S. Walter • Donal Skelly • Sue Ann Costa Clemens • Felipe Gomes Naveca • Valdinete Nascimento • Fernanda Nascimento • Cristiano Fernandes da Costa • Paola C. Resende • Alex Pauvolid-Correa • Marilda M. Siqueira • Christina Dold • Robert Levin • Tao Dong • Andrew J. Pollard • Julian C. Knight • Derrick Crook • Teresa Lambe • Elizabeth Clutterbuck • Sagida Bibi • Amy Flaxman • Mustapha Bittaye • Sandra Belij-Rammerstorfer • Sarah Gilbert • Miles W. Carroll • Paul Klenerman • Eleanor Barnes • Susanna J. Dunachie • Neil G. Paterson • Mark A. Williams • David R. Hall • Ruben J.G. Hulswit • Thomas A. Bowden • Elizabeth E. Fry • Juthathip Mongkolsapaya <u></u> • Jingshan Ren <u></u> • David I. Stuart <u></u>Gavin R. Screaton <u></u> • Show less • Show footnotes

Open Access • Published: March 30, 2021 • DOI: https://doi.org/10.1016/j.cell.2021.03.055

### **Highlights**

- 1 Despite similar RBD mutations P.1 is easier to neutralize than B.1.351.
- 2 P.1, B.1.351 and B.1.1.7 partially or fully escape most VH3-53 antibodies.
- 3 mAb 222 (VH3-53) retains neutralisation against all 3 variants.
- 4 Neutralisation is restored in VH3-53 chimeric antibodies with mAb 222 LC.

https://www.cell.com/cell/fulltext/S0092-8674(21)00428-1







## Impact of variants on the Oxford/Astrazeneca/Fiocruz Vaccine

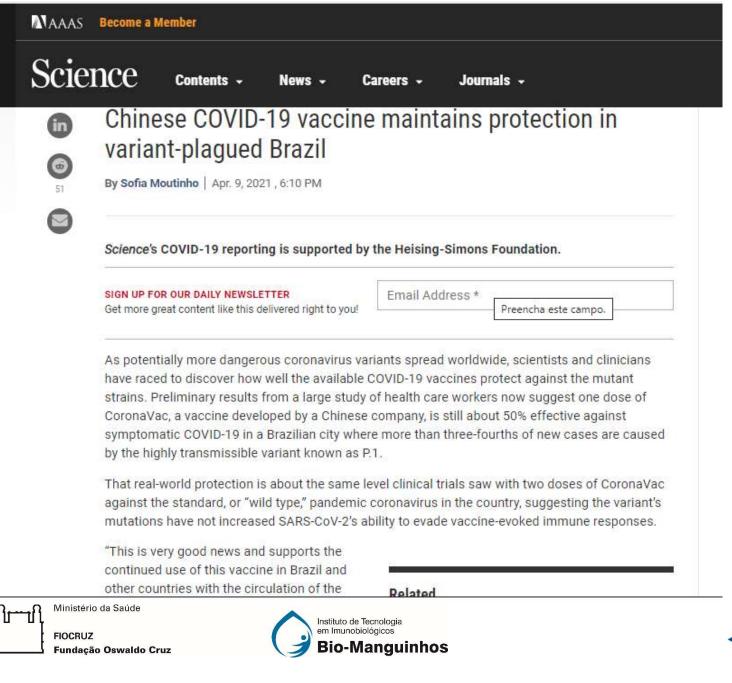
Variant Analyzed	B.1.351 (501Y.V2)	B.1.1.7 VOC 202012/01	P.1	B.1.351 e B.1.1.7		
Major Mutation	RBD (n=3) – the N501Y mutation is associated with increased affinity for the ACE2 receptor NTD (n = 5) - mutations E484K and K417N are associated with the escape of neutralizing antibodies.	N501Y is associated with increased affinity for the ACE2 receptor. Deletion in the protein Spike (nucleotides 69-70) associated with viral escape of antibodies. P681H associated with increased cell membrane fusion (in vitro)	RBD (n=3) - K417T and E484K have been shown in previous studies to promote antibody binding resistance, and the N501Y mutation is associated with increased affinity for the ACE2 receptor.	Substitution (Wahan AA numbering) L18F HV69-70del D80A V144del D215G LAL242-244del K417N E484K N501Y A570D D614G P681D A701V T716I S982A D1118H	VOC 8.1.1.7 <sup>1</sup>	VOC 8.1.351 + + + + + + + + + + + + + + + + + + +
Variant Origin	South Africa	UK	Brazil	South Africa and UK		
Pre-print	02/12/2021 Safety and efficacy of the ChAdOx1 nCoV-19 (AZD1222) Covid-19 vaccine against the B.1.351	02/04/2021 Efficacy of ChAdOx1 nCoV-19 (AZD1222) Vaccine Against SARS- CoV-2 VOC 202012/01 (B.1.1.7)	03/19/2021 Antibody evasion by the Brazilian P.1 strain of SARS- CoV-2	ChAdOx1 nCoV-19 (AZD1222) protects hamsters against SARS- CoV-2 B.1.351 and B.1.1.7 disease		
Paper	03/16/2021 Efficacy of the ChAdOx1 nCoV- 19 Covid-19 Vaccine against the B.1.351 Variant			~ _		



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Coronavirus variants: What are they and how do they happen?

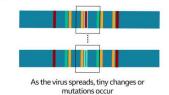
#### (1) High numbers of cases increase risk of mutations

The more a virus spreads, the more chance it has to mutate. Thousands of small changes have been seen in coronavirus so far - most with little impact.



#### 2 Some mutations lead to new variants

Every so often, a virus changes in a way that helps it survive and reproduce. These successful variants can become the dominant type.



#### (3) Three key variants are spreading more easily

Multiple coronavirus variants are circulating globally. Experts are concerned about three with changes to the virus's spike protein, the part that helps it enter human cells.

The genetic code for each of these variants is slightly different. N501Y UK "Kent" variant B.1.1.7

↓ N501Y↓ E484K South Africa variant B.1.351 ↓ N501Y↓ E484K Brazil variant P.1

N501Y mutation seen in UK, South Africa and Brazil variants may help the virus spread more easily. E484K mutation seen in South Africa, Brazil and some UK variants may affect the antibody response.

#### (4) Vaccines adapted to tackle variants

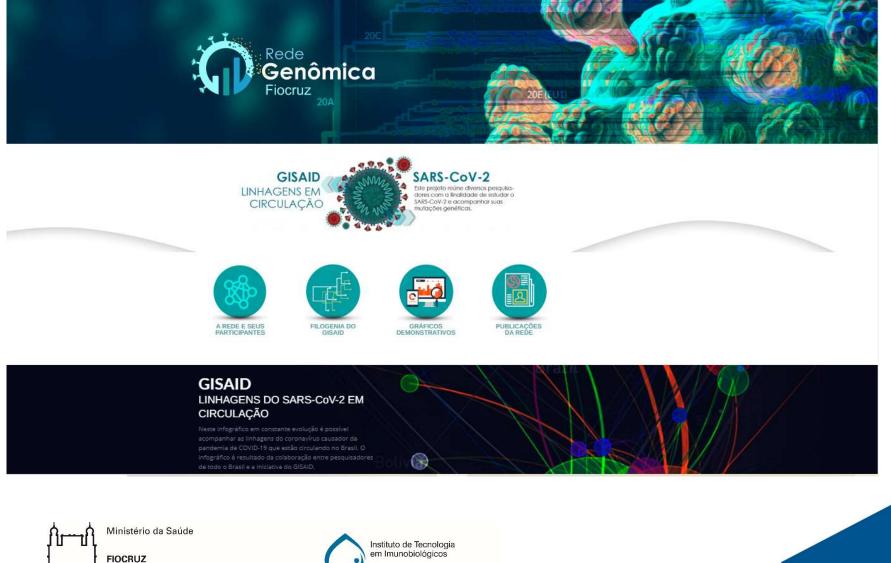
More variants will continue to emerge, but vaccines can be tweaked to better match them if needed.





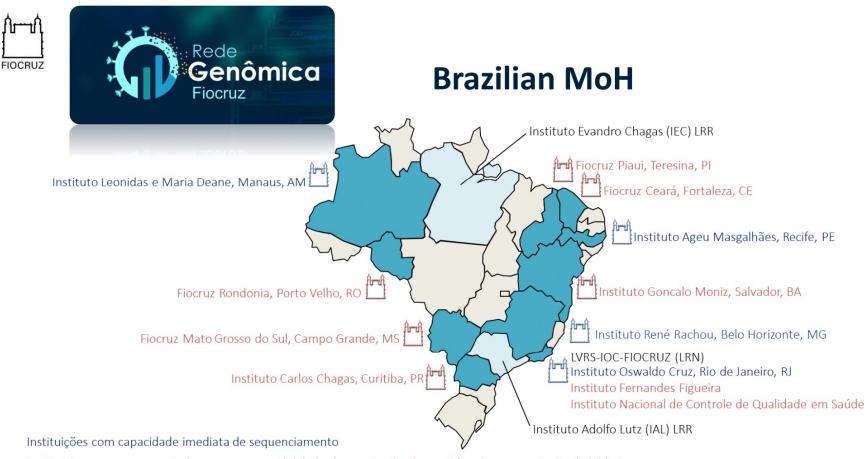
BBC





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#### http://www.genomahcov.fiocruz.br/

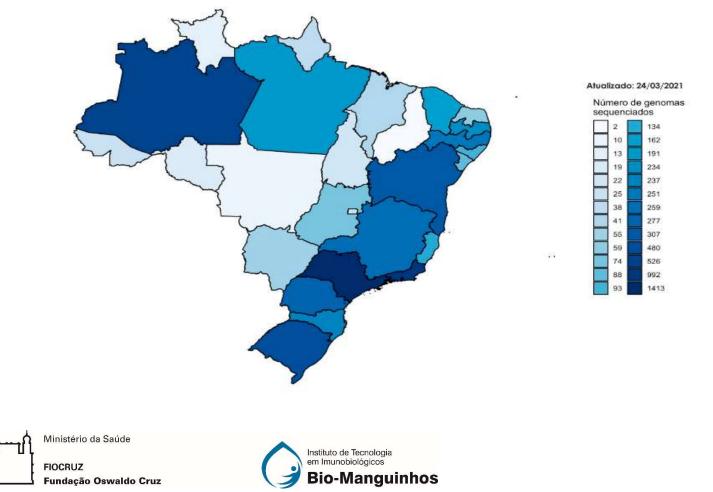






### Genomes generated from basil samples deposited at GISAID

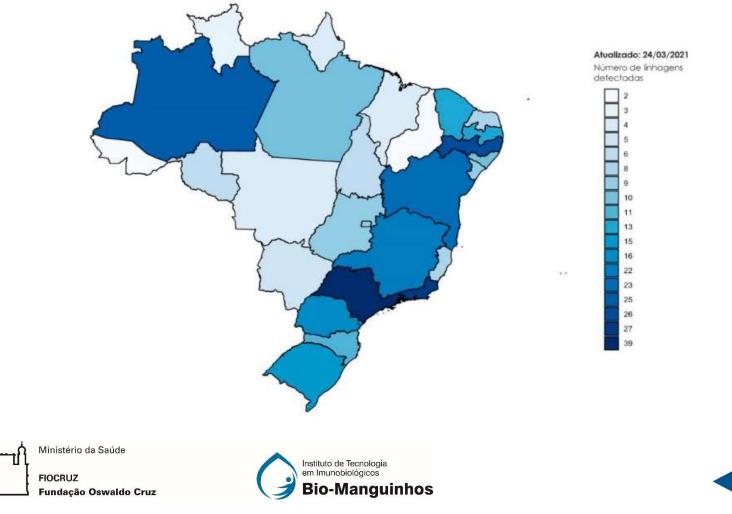
Data generated by the Fiocruz genomic network and / or deposited on the GISAID platform





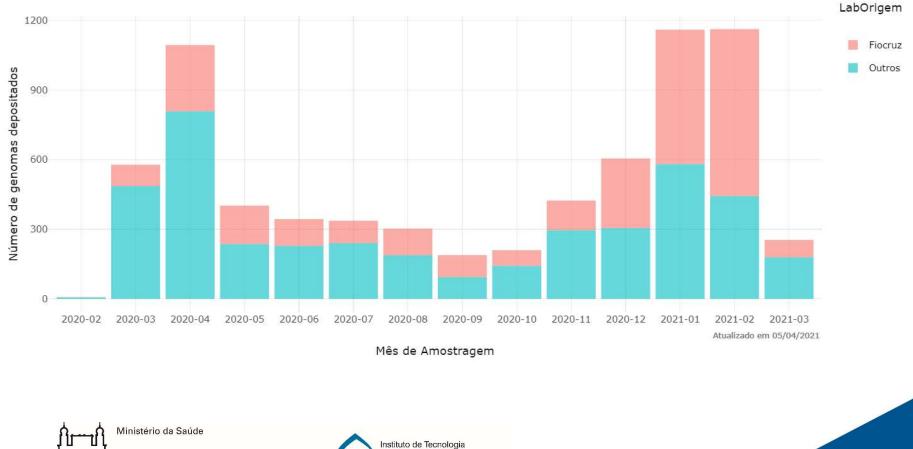
## Diversity of strains detected in Brazil

Data generated by the Fiocruz genomic network and / or deposited on the GISAID





## By month of collection



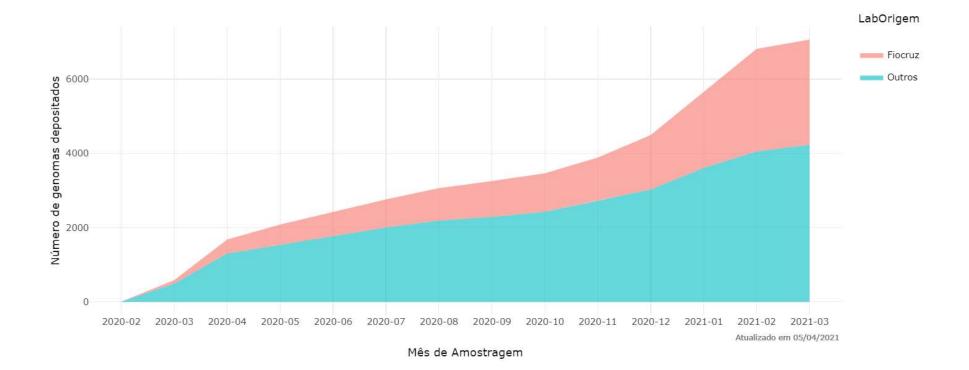
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## Accumulated

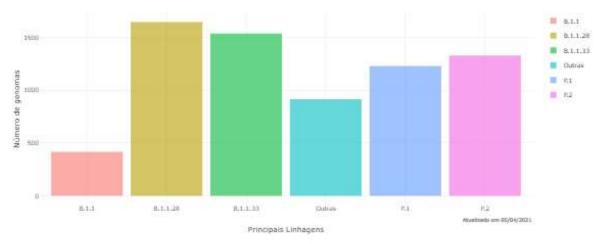


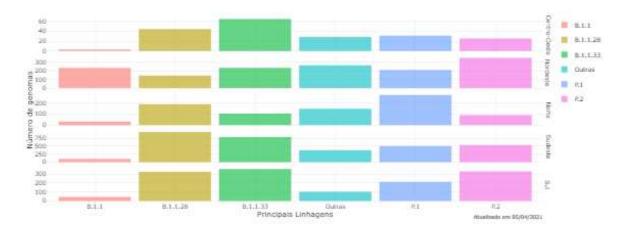




### Main strains of SARS Covid -2 found in Brazil

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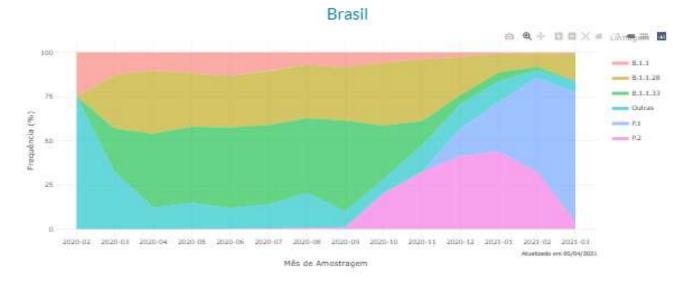




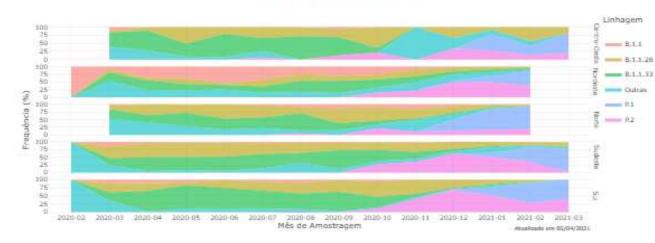


## Sampling

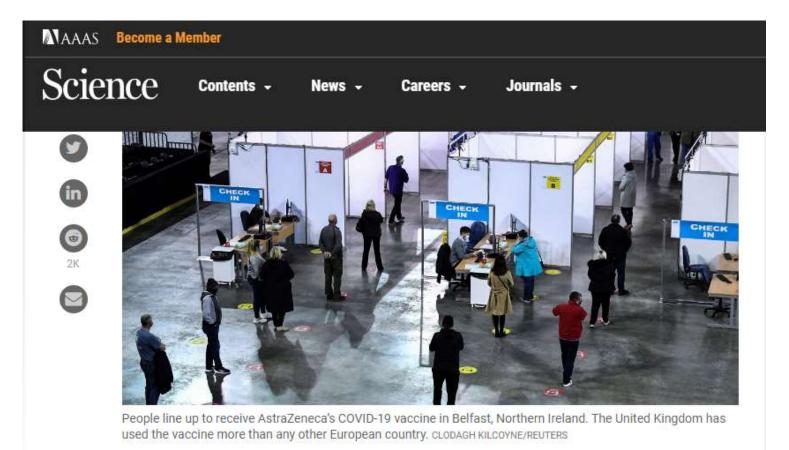
### Data generated by the Fiocruz genomic network and / or deposited on the GISAID platform



#### Por região geográfica







## Hard choices emerge as link between AstraZeneca vaccine and rare clotting disorder becomes clearer

By Kai Kupferschmidt, Gretchen Vogel | Apr. 11, 2021, 7:15 AM







The New York Times

### Blood Clots Linked to AstraZeneca Vaccine Stem From Rare Antibody Reaction

New studies from Germany and Norway examined cases involving mostly younger people who developed serious and sometimes fatal blood disorders.

#### f 🖸 ¥ 🛎 🄶 🗌



A dose of the AstraZeneca vaccine being administered in Bucharest, Romania, in February. The vaccine has been a mainstay of inoculation programs in more than 100 countries. Vadim Ghirda/Associated Press

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## Covid-19 Vaccine (recombinant)

**TECH TRANSFER ASTRAZENECA – Bio-Manguinhos/Fiocruz** 

✓ 4 million Doses received from Serum Institute – Marketing Authorization issued by Anvisa for Emergencial Use

✓ In March 12, 2021 Bio-Manguinhos received the definitive Marketing Authorization – Rolling Submission

1<sup>st</sup> Step of Tech Transfer - Bio-Manguinhos receives the API from Wuxi, performs the formulation, filling, Quality Control and Quality Assurance – Release the vaccine for NIP.



 ✓ From September, 2021 the API will be produced at Bio-Manguinhos Facility – The COVID-19 VACCINE (RECOMBINANT) will be completely nationalized





## Covid-19 Vaccine (recombinant)

Adverse Event Post Commercialization

Package Insert UPDATE

### Thrombosis and thrombocytopenia

"Very rare events of severe thrombosis with thrombocytopenia, including unusual sites, such as cerebral venous sinus thrombosis and splenic vein thrombosis, some associated with arterial thrombosis, have been observed after vaccination with the covid-19 (recombinant) vaccine during post-commercialization. Most events occurred in the first 14 days after vaccination and some events had a fatal outcome. Based on the available data, a causal relationship has not been established.

Health professionals should be aware of the signs and symptoms of thromboembolism and thrombocytopenia, as well as coagulopathies. Vaccinated individuals should be instructed to seek immediate medical attention if they develop symptoms such as severe or persistent headaches, blurred vision, shortness of breath, chest pain, leg swelling, persistent abdominal pain or unusual skin bruises and / or petechiae a few days later vaccination."









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# Thank you!

### Marcos da Silva Freire, DSc.



