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.
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


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https://www.researchsquare.com/article/rs-275494/v1
Novel SARS-CoV-2 Variant in Travelers from Brazil to Japan

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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.
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

Felipe Naveca 1, Valdinete Nascimento 1, Victor Souza 1, André Corado 1, Fernanda Nascimento 1, George Silva 1, Âgatha Costa 1, Débora Duarte 1, Karina Pessoa 1, Luciana Gonçalves 2, Maria Júlia Brandão 1, Michele Jesus 3, Cristiano Fernandes 2, Rosemary Pinto 2, Marineide Silva 4, Tirza Mattos 4, Gabriel Luz Wallau 5, Marlida Mendonça Siqueira 6, Paola Cristina Resende 6*, Edson Delatorre 7*, Tiago Gráf 8*, Gonzalo Bello 9*  
*These authors contributed equally to this work

Amazonian
Main Lineages in Brazil – update March 2021

Source: Fiocruz Coronavirus Genomic Network, MoH - Brazil and all Brazilian groups that contribute to GISAID initiative. (Last update 16th March 2021)
RESEARCH ARTICLE

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


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https://www.researchsquare.com/article/rs-318392/v1
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 3; 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 Lodal Florentino Teixeira 7; Irina Riediger 8; Maria do Carmo Deburn 8; Rodrigo Ribeiro-Rodrigues 9; Anderson Brandão Leite 10; Clíomar 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 Sachchi 17; Tizá Mattos 18; Cristiano Fernandes da Costa 19; Edson Delatorre 20*; Gabriel I Wallau 21*; Felipe G Naveca 22*; Gonzalo Bello 23*; Marilda Mendonça Siqueira 1* on behalf of Fiocruz COVID-19 Genomic Surveillance Network

N.9

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

<table>
<thead>
<tr>
<th>Genomic region (protein)</th>
<th>Nucleotide</th>
<th>Amino acid</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORF1a</td>
<td>G1264T</td>
<td>-</td>
</tr>
<tr>
<td>ORF1a</td>
<td>C7600T</td>
<td>-</td>
</tr>
<tr>
<td>ORF1a (NSP3)</td>
<td>C7851T</td>
<td>A2529V (A1711V)</td>
</tr>
<tr>
<td>ORF1a (NSP6)</td>
<td>T11078C</td>
<td>F3605L (F36L)</td>
</tr>
<tr>
<td>Spike (S)</td>
<td>G23012A</td>
<td>E484K</td>
</tr>
<tr>
<td>ORF7b (NSP7b)</td>
<td>A27853C</td>
<td>E33A</td>
</tr>
</tbody>
</table>

Now accepted for publication in Viruses
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


<table>
<thead>
<tr>
<th>Sample(s)</th>
<th>Lineage</th>
<th>NTD Indel</th>
<th>RBD</th>
<th>GISAID ID</th>
</tr>
</thead>
<tbody>
<tr>
<td>AM-FIOCRUZ-20842572LS/2020*</td>
<td>P.1</td>
<td>A144</td>
<td></td>
<td>EPI ISL_1068132</td>
</tr>
<tr>
<td>MO-FIOCRUZ-6180/2021*</td>
<td>P.2</td>
<td>A144</td>
<td>E484K</td>
<td>EPI ISL_1219137</td>
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<tr>
<td>BA53/2021*</td>
<td>P.1</td>
<td>A144</td>
<td>K417T</td>
<td>EPI ISL_1067720</td>
</tr>
<tr>
<td>BA54/2021*</td>
<td></td>
<td></td>
<td>E484K</td>
<td>EPI ISL_1067733</td>
</tr>
<tr>
<td>BA55/2021*</td>
<td></td>
<td></td>
<td>N501Y</td>
<td>EPI ISL_1067734</td>
</tr>
<tr>
<td>BA-FIOCRUZ-7029/2021*</td>
<td></td>
<td></td>
<td>E484K</td>
<td>EPI ISL_1219134</td>
</tr>
<tr>
<td>AL-FIOCRUZ-4795/2021*</td>
<td>P.1</td>
<td>A141-144</td>
<td>K417T</td>
<td>EPI ISL_1219134</td>
</tr>
<tr>
<td>PR-FIOCRUZ-5273/2021**</td>
<td></td>
<td></td>
<td>E484K</td>
<td>EPI ISL_1219134</td>
</tr>
<tr>
<td>AL-FIOCRUZ-4786/2021*</td>
<td>P.1</td>
<td>A189-190</td>
<td>K417T</td>
<td>EPI ISL_1219135</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>E484K</td>
<td>EPI ISL_1181371</td>
</tr>
<tr>
<td>MA-FIOCRUZ-6871/2021</td>
<td>B.1.1.33 (E484K)</td>
<td>A141-144</td>
<td>V445A</td>
<td>EPI ISL_1181370</td>
</tr>
<tr>
<td>MA-FIOCRUZ-4674/2021</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AM-FIOCRUZ-208972690P*</td>
<td>B.1.1.33 (E484K)</td>
<td>A141-144</td>
<td>V445A</td>
<td>EPI ISL_1068256</td>
</tr>
<tr>
<td>AM-FIOCRUZ-20897281WS*</td>
<td>(P1-like)</td>
<td>A256-258</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AM-FIOCRUZ-21846595CL*</td>
<td>(P1-like)</td>
<td>A256-258</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PR-FIOCRUZ-5241/2021</td>
<td></td>
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</tbody>
</table>
Antibody evasion by the P.1 strain of SARS-CoV-2


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

<table>
<thead>
<tr>
<th>Variant Analyzed</th>
<th><strong>B.1.351 (501Y.V2)</strong></th>
<th><strong>B.1.1.7 VOC 202012/01</strong></th>
<th><strong>P.1</strong></th>
<th><strong>B.1.351 e B.1.1.7</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Major Mutation</strong></td>
<td>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.</td>
<td>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)</td>
<td>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.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Variant Origin</th>
<th>South Africa</th>
<th>UK</th>
<th>Brazil</th>
<th>South Africa and UK</th>
</tr>
</thead>
</table>
| **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 | - | - | - |
Chinese COVID-19 vaccine maintains protection in variant-plagued Brazil

By Sofia Moutinho | Apr. 9, 2021, 6:10 PM

As potentially more dangerous coronavirus variants spread worldwide, scientists and clinicians have raced to discover how well the available COVID-19 vaccines protect against the mutant strains. Preliminary results from a large study of healthcare workers now suggest one dose of CoronaVac, a vaccine developed by a Chinese company, is still about 50% effective against symptomatic COVID-19 in a Brazilian city where more than three-fourths of new cases are caused by the highly transmissible variant known as P.1.

That real-world protection is about the same level clinical trials saw with two doses of CoronaVac against the standard, or "wild type," pandemic coronavirus in the country, suggesting the variant's mutations have not increased SARS-CoV-2's ability to evade vaccine-evoked immune responses.

"This is very good news and supports the continued use of this vaccine in Brazil and other countries with the circulation of the
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.

- UK "Kent" variant B.1.1.7
- South Africa variant B.1.351
- Brazil variant P.1

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

Source: Centers for Disease Control and Prevention, BBC research
GISAID
LINHAGENS DO SARS-CoV-2 EM CIRCULAÇÃO

Neste infográfico, em constante evolução, é possível acompanhar a linhagem do coronavírus causador da pandemia de COVID-19 que estão circulando no Brasil. O infográfico é resultado da colaboração entre pesquisadores do Mיסטério da Saúde e other publicações de GISAID.
Brazilian MoH

Instituícios com capacidade imediata de sequenciamento
Instituícios a serem capacitadas mas com possibilidade de construção de amplificação ou construção de bibliotecas

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 platform
By month of collection
Accumulated
Main strains of SARS Covid-2 found in Brazil

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

Data generated by the Fiocruz genominc network and/or deposited on the GISAID platform
People line up to receive AstraZeneca's COVID-19 vaccine in Belfast, Northern Ireland. The United Kingdom has used the vaccine more than any other European country. CLOGASH KILCOYNE/REUTERS

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
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.
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

1st 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.

100,4 million doses will be released until July, 2021

- From September, 2021 the API will be produced at Bio-Manguinhos Facility – The COVID-19 VACCINE (RECOMBINANT) will be completely nationalized
“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.”
Thank you!

Marcos da Silva Freire, DSc.