

## Boletim BiblioCovid

Boletim BiblioCovid v.2 n.9, setembro 2021 | Variantes da Covid-19

Boletim destinado a apresentação de estratégias e artigos científicos sobre temas relacionados à Covid-19.

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## Variantes da Covid-19



### Vocabulário controlado

MeSH – Medical Subject Headings (NLM/NIH)  
DeCS

### Bases utilizadas

HISA - base bibliográfica em história da saúde pública na América Latina e Caribe (Acesso via portal Regional BVS)

### Termos Utilizados (com base no Medical Subject Headings – MeSH):

#### Descritores e/ou palavras-chave

New Coronavirus  
Novel Coronavirus  
Nuevo Coronavirus  
Novo Coronavirus  
Coronavirus disease  
2019-ncov  
ncov 2019  
2019ncov  
Covid19  
covid-19  
covid 2019

srag-cov-2  
sars-cov-2  
Sars2  
sars 2  
sars cov 2  
cov19  
Cov2019  
Coronavirus\*  
Coronavirus 2  
Covid2019  
covid-2019

#### Filtros utilizados

Artigos (tipo de documento)  
Medline (base de dados)



### Estratégias de busca

((variant\*) (((("2019-2020" OR 2019 OR da:202\*) ("New Coronavirus" OR "Novel Coronavirus" OR "Nuevo Coronavirus" OR "Novo Coronavirus" OR "Coronavirus disease" OR "Enfermedad por Coronavirus" OR "severe acute respiratory syndrome coronavirus 2")) OR ((2019-ncov) OR (ncov 2019) OR 2019ncov OR covid19 OR (covid-19) OR covid2019 OR (covid-2019) OR (covid 2019)) OR ((srag-cov-2 OR sars-cov-2 OR sars2 OR (sars 2) OR (sars cov 2) OR cov19 OR cov2019 OR Coronavirus\* OR "Severe Acute Respiratory Infections" OR "Severe Acute Respiratory Infection" OR "Coronavirus 2" OR "acute respiratory disease" OR mh:Betacoronavirus OR mh:"Coronavirus infections" OR mh:"sars virus") AND (tw:2019 OR da:202\*) AND NOT da:201\*) OR (Wuhan market virus) OR (virus mercado Wuhan) OR "Wuhan Coronavirus" OR "Coronavirus de Wuhan") AND NOT (ti:dromedar\*)))

Seleção dos dez artigos mais relevantes, segundo critérios da base de dados Portal regional BVS, incluindo o filtro "Artigo (tipo de documento)" e "Medline (base de dados)"

## 1. Early introductions and transmission of SARS-CoV-2 variant B.1.1.7 in the United States

[doi:https://doi.org/10.1016/j.cell.2021.03.061](https://doi.org/10.1016/j.cell.2021.03.061)

### Resumo

The emergence and spread of SARS-CoV-2 lineage B.1.1.7, first detected in the United Kingdom, has become a global public health concern because of its increased transmissibility. Over 2,500 COVID-19 cases associated with this variant have been detected in the United States (US) since December 2020, but the extent of establishment is relatively unknown. Using travel, genomic, and diagnostic data, we highlight that the primary ports of entry for B.1.1.7 in the US were in New York, California, and Florida. Furthermore, we found evidence for many independent B.1.1.7 establishments starting in early December 2020, followed by interstate spread by the end of the month. Finally, we project that B.1.1.7 will be the dominant lineage in many states by mid- to late March. Thus, genomic surveillance for B.1.1.7 and other variants urgently needs to be enhanced to better inform the public health response.

### Referência

ALPERT, T. et al. Early introductions and transmission of SARS-CoV-2 variant B.1.1.7 in the United States. **Cell**, v. 184, n. 10, p. 2595-2604, May 2021. Disponível em: <<https://www.sciencedirect.com/science/article/pii/S0092867421004347>>. Acesso em: 21 jul. 2021.

## 2. Emergence and rapid transmission of SARS-CoV-2 B.1.1.7 in the United States

[doi:https://doi.org/10.1016/j.cell.2021.03.052](https://doi.org/10.1016/j.cell.2021.03.052)

### Resumo

The highly transmissible B.1.1.7 variant of SARS-CoV-2, first identified in the United Kingdom, has gained a foothold across the world. Using S gene target failure (SGTF) and SARS-CoV-2 genomic sequencing, we investigated the prevalence and dynamics of this variant in the United States (US), tracking it back to its early emergence. We found that, while the fraction of B.1.1.7 varied by state, the variant increased at a logistic rate with a roughly weekly doubling rate and an increased transmission of 40%-50%. We revealed several independent introductions of B.1.1.7 into the US as early as late November 2020, with community transmission spreading it to most states within months. We show that the US is on a similar trajectory as other countries where B.1.1.7 became dominant, requiring immediate and decisive action to minimize COVID-19 morbidity and mortality.

### Referência

WASHINGTON, N. L. et al. Emergence and rapid transmission of SARS-CoV-2 B.1.1.7 in the United States. **Cell**, v. 184, n. 10, p. 2587-2594, May 2021. Disponível em: < <https://pubmed.ncbi.nlm.nih.gov/33861950> >. Acesso em: 21 jul. 2021.

## 3. Evidence of escape of SARS-CoV-2 variant B.1.351 from natural and vaccine-induced sera

[doi:https://doi.org/10.1016/j.cell.2021.02.037](https://doi.org/10.1016/j.cell.2021.02.037)

### Resumo

The race to produce vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) began when the first sequence was published, and this forms the basis for vaccines currently deployed globally. Independent lineages of SARS-CoV-2 have recently been reported UK, B.1.1.7; South Africa, B.1.351; and Brazil, P.1. These variants have multiple changes in the immunodominant spike protein that facilitates viral cell entry via the angiotensin-converting enzyme-2 (ACE2) receptor. Mutations in the receptor recognition site on the spike are of great concern for their potential for immune escape. Here, we describe a structure-function analysis of B.1.351 using a large cohort of convalescent and vaccinee serum samples. The receptor-binding domain mutations provide tighter ACE2 binding and widespread escape from monoclonal antibody neutralization largely driven by E484K, although K417N and N501Y act together against some important antibody classes. In a number of cases, it would appear that convalescent and some vaccine serum offers limited protection against this variant.

### Referência

ZHOU, D. et al. Evidence of escape of SARS-CoV-2 variant B.1.351 from natural and vaccine-induced sera. **Cell**, v. 189, n. 9, p. 2348-2361, April 2021. Disponível em: <https://www.sciencedirect.com/science/article/pii/S0092867421002269>. Acesso em: 21 jul. 2021.

## 4. SARS-CoV-2 variants B.1.351 and P.1 escape from neutralizing antibodies

[doi:https://doi.org/10.1016/j.cell.2021.03.036](https://doi.org/10.1016/j.cell.2021.03.036)

### Resumo

The global spread of SARS-CoV-2/COVID-19 is devastating health systems and economies worldwide. Recombinant or vaccine-induced neutralizing antibodies are used to combat the COVID-19 pandemic. However, the recently emerged SARS-CoV-2 variants B.1.1.7 (UK), B.1.351 (South Africa), and P.1 (Brazil) harbor mutations in the viral spike (S) protein that may alter virus-host cell interactions and confer resistance to inhibitors and antibodies. Here, using pseudoparticles, we show that entry of all variants into human cells is susceptible to blockade by the entry inhibitors soluble ACE2, Camostat, EK-1, and EK-1-C4. In contrast, entry of the B.1.351 and P.1 variant was partially (Casirivimab) or fully (Bamlanivimab) resistant to antibodies used for COVID-19 treatment. Moreover, entry of these variants was less efficiently inhibited by plasma from convalescent COVID-19 patients and sera from BNT162b2-vaccinated individuals. These results suggest that SARS-CoV-2 may escape neutralizing antibody responses, which has important implications for efforts to contain the pandemic.

### Referência

HOFFMANN, M. et al. SARS-CoV-2 variants B.1.351 and P.1 escape from neutralizing antibodies. *Cell*, v. 184, n. 9, p. 2384-2393, April 2021. Disponível em: <https://pubmed.ncbi.nlm.nih.gov/33794143/>. Acesso em: 21 jul. 2021.

## 5. Transmission, infectivity, and neutralization of a spike L452R SARS-CoV-2 variant

[doi:https://doi.org/10.1016/j.cell.2021.04.025](https://doi.org/10.1016/j.cell.2021.04.025)

### Resumo

We identified an emerging severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variant by viral whole-genome sequencing of 2,172 nasal/nasopharyngeal swab samples from 44 counties in California, a state in the western United States. Named B.1.427/B.1.429 to denote its two lineages, the variant emerged in May 2020 and increased from 0% to >50% of sequenced cases from September 2020 to January 2021, showing 18.6%-24% increased transmissibility relative to wild-type circulating strains. The variant carries three mutations in the spike protein, including an L452R substitution. We found 2-fold increased B.1.427/B.1.429 viral shedding in vivo and increased L452R pseudovirus infection of cell cultures and lung organoids, albeit decreased relative to pseudoviruses carrying the N501Y mutation common to variants B.1.1.7, B.1.351, and P.1. Antibody neutralization assays revealed 4.0- to 6.7-fold and 2.0-fold decreases in neutralizing titers from convalescent patients and vaccine recipients, respectively. The increased prevalence of a more transmissible variant in California exhibiting decreased antibody neutralization warrants further investigation.

### Referência

DENG, X. et al. Transmission, infectivity, and neutralization of a spike L452R SARS-CoV-2 variant. **Cell**, v. 184, n. 13, p. 3426-3437, 2021. Disponível em: <https://pubmed.ncbi.nlm.nih.gov/33991487/>. Acesso em: 21 jul. 2021.

## 6. Public health actions to control new SARS-CoV-2 variants

[doi:https://doi.org/10.1016/j.cell.2021.01.044](https://doi.org/10.1016/j.cell.2021.01.044)

### Resumo

Analisa Recent reports suggest that some SARS-CoV-2 genetic variants, such as B.1.1.7, might be more transmissible and are quickly spreading around the world. As the emergence of more transmissible variants could exacerbate the pandemic, we provide public health guidance for increased surveillance and measures to reduce community transmission.

### Referência

GRUBAUGH, N. D. et al. Public health actions to control new SARS-CoV-2 variants. **Cell**, v. 184, n. 5, p. 1127-1132, 2021. Disponível em: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7846239/>. Acesso em: 21 jul. 2021.

## 7. N-terminal domain antigenic mapping reveals a site of vulnerability for SARS-CoV-2

[doi:https://doi.org/10.1016/j.cell.2021.03.028](https://doi.org/10.1016/j.cell.2021.03.028)

### Resumo

The SARS-CoV-2 spike (S) glycoprotein contains an immunodominant receptor-binding domain (RBD) targeted by most neutralizing antibodies (Abs) in COVID-19 patient plasma. Little is known about neutralizing Abs binding to epitopes outside the RBD and their contribution to protection. Here, we describe 41 human monoclonal Abs (mAbs) derived from memory B cells, which recognize the SARS-CoV-2 S N-terminal domain (NTD) and show that a subset of them neutralize SARS-CoV-2 ultrapotently. We define an antigenic map of the SARS-CoV-2 NTD and identify a supersite (designated site i) recognized by all known NTD-specific neutralizing mAbs. These mAbs inhibit cell-to-cell fusion, activate effector functions, and protect Syrian hamsters from SARS-CoV-2 challenge, albeit selecting escape mutants in some animals. Indeed, several SARS-CoV-2 variants, including the B.1.1.7, B.1.351, and P.1 lineages, harbor frequent mutations within the NTD supersite, suggesting ongoing selective pressure and the importance of NTD-specific neutralizing mAbs for protective immunity and vaccine design.

### Referência

MCCALLUM, M. et al. N-terminal domain antigenic mapping reveals a site of vulnerability for SARS-CoV-2. **Cell**, v. 184, n. 9, p. 2332-2347, 2021. Disponível em: <<https://pubmed.ncbi.nlm.nih.gov/33761326/>>. Acesso em: 21 jul. 2021.



## 8. Circulating SARS-CoV-2 spike N439K variants maintain fitness while evading antibody-mediated immunity

[doi:https://doi.org/10.1016/j.cell.2021.01.037](https://doi.org/10.1016/j.cell.2021.01.037)

### Resumo

SARS-CoV-2 can mutate and evade immunity, with consequences for efficacy of emerging vaccines and antibody therapeutics. Here, we demonstrate that the immunodominant SARS-CoV-2 spike (S) receptor binding motif (RBM) is a highly variable region of S and provide epidemiological, clinical, and molecular characterization of a prevalent, sentinel RBM mutation, N439K. We demonstrate N439K S protein has enhanced binding affinity to the hACE2 receptor, and N439K viruses have similar in vitro replication fitness and cause infections with similar clinical outcomes as compared to wild type. We show the N439K mutation confers resistance against several neutralizing monoclonal antibodies, including one authorized for emergency use by the US Food and Drug Administration (FDA), and reduces the activity of some polyclonal sera from persons recovered from infection. Immune evasion mutations that maintain virulence and fitness such as N439K can emerge within SARS-CoV-2 S, highlighting the need for ongoing molecular surveillance to guide development and usage of vaccines and therapeutics.

### Referência

THOMSON, E. C. et al. Circulating SARS-CoV-2 spike N439K variants maintain fitness while evading antibody-mediated immunity. **Cell**, v. 184, n. 5, p. 1171-1187, 2021. Disponível em: <https://pubmed.ncbi.nlm.nih.gov/33621484/>. Acesso em: 21 jul. 2021.

## 9. Multiple SARS-CoV-2 variants escape neutralization by vaccine-induced humoral immunity

[doi:https://doi.org/10.1016/j.cell.2021.03.013](https://doi.org/10.1016/j.cell.2021.03.013)

### Resumo

Vaccination elicits immune responses capable of potently neutralizing SARS-CoV-2. However, ongoing surveillance has revealed the emergence of variants harboring mutations in spike, the main target of neutralizing antibodies. To understand the impact of these variants, we evaluated the neutralization potency of 99 individuals that received one or two doses of either BNT162b2 or mRNA-1273 vaccines against pseudoviruses representing 10 globally circulating strains of SARS-CoV-2. Five of the 10 pseudoviruses, harboring receptor-binding domain mutations, including K417N/T, E484K, and N501Y, were highly resistant to neutralization. Cross-neutralization of B.1.351 variants was comparable to SARS-CoV and bat-derived WIV1-CoV, suggesting that a relatively small number of mutations can mediate potent escape from vaccine responses. While the clinical impact of neutralization resistance remains uncertain, these results highlight the potential for variants to escape from neutralizing humoral immunity and emphasize the need to develop broadly protective interventions against the evolving pandemic.

### Referência

GARCIA-BELTRAN, W. F. et al. Multiple SARS-CoV-2 variants escape neutralization by vaccine-induced humoral immunity. **Cell**, v. 184, n. 9, p. 2372-2383, 2021. Disponível em: <https://pubmed.ncbi.nlm.nih.gov/33743213/>. Acesso em: 21 jul. 2021.

## 10. Evaluating the Effects of SARS-CoV-2 Spike Mutation D614G on Transmissibility and Pathogenicity

[doi:https://doi.org/10.1016/j.cell.2020.11.020](https://doi.org/10.1016/j.cell.2020.11.020)

### Resumo

Global dispersal and increasing frequency of the SARS-CoV-2 spike protein variant D614G are suggestive of a selective advantage but may also be due to a random founder effect. We investigate the hypothesis for positive selection of spike D614G in the United Kingdom using more than 25,000 whole genome SARS-CoV-2 sequences. Despite the availability of a large dataset, well represented by both spike 614 variants, not all approaches showed a conclusive signal of positive selection. Population genetic analysis indicates that 614G increases in frequency relative to 614D in a manner consistent with a selective advantage. We do not find any indication that patients infected with the spike 614G variant have higher COVID-19 mortality or clinical severity, but 614G is associated with higher viral load and younger age of patients. Significant differences in growth and size of 614G phylogenetic clusters indicate a need for continued study of this variant.

### Referência

VOLZ, E. et al. Evaluating the Effects of SARS-CoV-2 Spike Mutation D614G on Transmissibility and Pathogenicity. **Cell**, v. 184, n. 1, p. 64-75, 2021. Disponível em: <<https://pubmed.ncbi.nlm.nih.gov/33275900>>. Acesso em: 21 jul. 2021.



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## Expediente

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**Imagens:** Pixabay

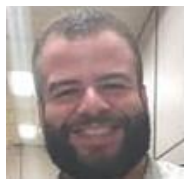
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