### COVID-19 Evidence Support Team

**EVIDENCE SEARCH REPORT**

<table>
<thead>
<tr>
<th>Review Question:</th>
<th>What is the epidemiology of variants and what are the implications for healthcare?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Context:</td>
<td>Update for ongoing review</td>
</tr>
<tr>
<td>Review Code:</td>
<td>EOC031801v11 ESR</td>
</tr>
<tr>
<td>Complete Date:</td>
<td>August 13, 2021</td>
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</tbody>
</table>

### Librarian Notes & Comments

Hello all,
Here is the update on the COVID-19 variants from July 31, 2021 to August 13, 2021 for the databases and the grey literature.

Sincerely,

Lukas and Brianna

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**Disclaimer**

This information is provided as a service by the Saskatchewan Health Authority and University of Saskatchewan Libraries. Professional librarians conduct searches of the literature. Results are subject to the limitations of the databases and the specificity, breadth and appropriateness of the search parameters presented by the requester. The Libraries do not represent in any matter that retrieved citations are complete, accurate or otherwise to be relied upon. The search results are only valid as of the date and time at which the search is conducted. The Libraries do not accept responsibility for any loss or damage arising from the use of, or reliance on, search results.
Search Results: Guidelines, Summaries & Other Grey Literature

Government
Public Health Ontario

PHAC Emerging Science Group

Public Health England
- SARS-CoV-2 variants of concern and variants under investigation in England

CDC
- Rapid Increase in Circulation of the SARS-CoV-2 B.1.617.2 (Delta) Variant — Mesa County, Colorado, April–June 2021. August 13, 2021. https://www.cdc.gov/mmwr/volumes/70/wr/mm7032e2.htm?s_cid=mm7032e2_w
- Rapid Increase in Circulation of the SARS-CoV-2 B.1.617.2 (Delta) Variant — Mesa County, Colorado, April–June 2021. August 13, 2021. https://www.cdc.gov/mmwr/volumes/70/wr/mm7032e2.htm?s_cid=mm7032e2_x

Agencies
WHO
Search Results: News, Blogs, & Social Media

News

CBC


CIDRAP


Search Results: Journal Articles (includes preprints)

Sorted by newest-oldest.


ABSTRACT: The sensitivity of molecular diagnostics could be affected by nucleotide variants in pathogen genes, and the sites affected by such variants should be monitored. We report a single-nucleotide variant (SNV) in the nucleocapsid (N) gene of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), i.e., G29179T, which impairs the diagnostic sensitivity of the Xpert Xpress SARS-CoV-2 assay (Cepheid, Sunnyvale, CA, USA). We observed significant differences between the threshold cycle (Ct) values for envelope (E) and N genes and confirmed the SNV as the cause of the differences using Sanger sequencing. This SNV, G29179T, is the most prevalent in Korea and is associated with the B.1.497 virus lineage, which is dominant in Korea. Clinical laboratories should be aware of the various SNVs in the SARS-CoV-2 genome and consider their potential effects on the diagnosis of coronavirus disease 2019.

**ABSTRACT:** Background The newly described SARS-CoV-2 lineage C.37 was recently classified as a variant of interest by the WHO (Lambda variant) based on its high circulation rates in South American countries and the presence of critical mutations in the spike protein. The impact of such mutations in infectivity and immune escape from neutralizing antibodies are entirely unknown. Methods We performed a pseudotyped virus neutralization assay and determined the impact of the Lambda variant on infectivity and immune escape using plasma samples from healthcare workers (HCW) from two centers in Santiago, Chile who received the two-doses scheme of the inactivated virus vaccine CoronaVac. Results We observed an increased infectivity mediated by the Lambda spike protein that was even higher than that of the D614G (lineage B) or the Alpha and Gamma variants. Compared to the Wild type (lineage A), neutralization was decreased by 3.05-fold for the Lambda variant while it was 2.33-fold for the Gamma variant and 2.03-fold for the Alpha variant. Conclusions Our results indicate that mutations present in the spike protein of the Lambda variant of interest confer increased infectivity and immune escape from neutralizing antibodies elicited by CoronaVac. These data reinforce the idea that massive vaccination campaigns in countries with high SARS-CoV-2 circulation must be accompanied by strict genomic surveillance allowing the identification of new isolates carrying spike mutations and immunology studies aimed to determine the impact of these mutations in immune escape and vaccines breakthrough. Competing Interest Statement The authors have declared no competing interest. Funding Statement ANID Chile supports the authors through Fondecyt grants numbers 1190156 (R.S.-R.), 1211547 (F.V.-E.) and 1181656 (A.G.) Author Declarations I confirm all relevant ethical guidelines have been followed, and any necessary IRB and/or ethics committee approvals have been obtained. Yes The details of the IRB/oversight body that provided approval or exemption for the research described are given below: The study protocol was approved by the Ethics Committee of the Faculty of Medicine at Universidad de Chile (Projects No 0361-2021 and No 096-2020) and Clínica Santa María (Project No132604-21). All participants signed the informed consent, and their samples were anonymized. All necessary patient/participant consent has been obtained and the appropriate institutional forms have been archived. Yes I understand that all clinical trials and any other prospective interventional studies must be registered with an ICMJE-approved registry, such as ClinicalTrials.gov. I confirm that any such study reported in the manuscript has been registered and the trial registration ID is provided (note: if posting a prospective study registered retrospectively, please provide a statement in the trial ID field explaining why the study was not registered in advance). Yes I have followed all appropriate research reporting guidelines and uploaded the relevant EQUATOR Network research reporting checklist(s) and other pertinent material as supplementary files, if applicable. Yes Data will be available upon request URL: http://medrxiv.org/content/early/2021/07/01/2021.06.28.21259673.abstract DOI: 10.1101/2021.06.28.21259673

3. Anonymous. Decreased neutralization of the Eta SARS-CoV-2 variant by sera of previously infected and uninfected vaccinated individuals. J Infect. 2021;06:06. DOI: 10.1016/j.jinf.2021.08.005

URL: https://www.ncbi.nlm.nih.gov/pubmed/34371077
DOI: 10.1016/j.jinf.2021.08.005
URL: https://www.ncbi.nlm.nih.gov/pubmed/34364949
DOI: 10.1016/j.jinf.2021.08.006

ABSTRACT: Considering the lack of effective treatments against COVID-19, wastewater-based epidemiology (WBE) is emerging as a cost-effective approach for real-time population-wide SARS-CoV-2 monitoring. Here, we report novel molecular assays for sensitive detection and mutational/variant analysis of SARS-CoV-2 in wastewater. Highly stable regions of SARS-CoV-2 RNA were identified by RNA stability analysis and targeted for the development of novel nested PCR assays. Targeted DNA sequencing (DNA-seq) was applied for the analysis and quantification of SARS-CoV-2 mutations/variants, following hexamers-based reverse transcription and nested PCR-based amplification of targeted regions. Three-dimensional (3D) structure models were generated to examine the predicted structural modification caused by genomic variants. WBE of SARS-CoV-2 revealed to be assay dependent, and significantly improved sensitivity achieved by assay combination (94%) vs. single-assay screening (30%-60%). Targeted DNA-seq allowed the quantification of SARS-CoV-2 mutations/variants in wastewater, which agreed with COVID-19 patients’ sequencing data. A mutational analysis indicated the prevalence of D614G (S) and P323L (RdRP) variants, as well as of the B.1.1.7/alpha variant of concern, in agreement with the frequency of B.1.1.7/alpha variant in clinical samples of the same period of the third pandemic wave at the national level. Our assays provide an innovative cost-effective platform for real-time monitoring and early-identification of SARS-CoV-2 variants at community/population levels. Copyright © 2021 by the authors. Licensee MDPI, Basel, Switzerland.

URL: https://www.ncbi.nlm.nih.gov/pubmed/34314049
DOI: 10.1002/jmv.27235

ABSTRACT: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) evolution is expected, given the nature of virus replication. Selection and establishment of variants in the human population depend on viral fitness and on molecular and immunological selection pressures. Here we discuss how mechanisms of replication and recombination may contribute to the emergence of current and future variants of SARS-CoV-2.
URL: https://www.ncbi.nlm.nih.gov/pubmed/34373192

DOI: 10.1136/bmj.n1960
URL: https://www.ncbi.nlm.nih.gov/pubmed/34373255
DOI: 10.1136/bmj.n1960
URL: https://www.ncbi.nlm.nih.gov/pubmed/34287620
DOI: 10.1001/jama.2021.11656

URL: https://www.ncbi.nlm.nih.gov/pubmed/34107199
DOI: 10.1056/NEJMp2103859

ABSTRACT: INTRODUCTION: Following the emergence of SARS-CoV-2 variants of concern (VOCs) worldwide, it is important to monitor local epidemiology to better understand the occurrence of clusters, reinfections, or infection after vaccination. Detecting mutations by specific RT-qPCR is a rapid and affordable alternative to sequencing. However, care must be taken to ensure that the techniques used are up-to-date and adapted to the variants circulating in the studied population. MATERIAL AND METHODS: All samples tested positive for SARS-CoV-2 were screened for detection of mutations of the spike protein using the Novaplex SARS-CoV-2 Variants I Assay from week 11 of 2021. Target sought were deletion H69/V70 and mutations N501Y and E484 K. From week 18 we used in addition the new Novaplex SARS-CoV-2 Variants II Assay for samples with no targets found with the Variants I assay or with the mutation E484 K alone, in order to screen the mutations L452R, K417 N/T and W152C. RESULTS: Between weeks 11 and 25, 2239 positive samples out of 54,317 were tested with the Variants I Assay. Between weeks 18 and 25, 94 samples met the criteria for being tested with the Variants II Assay. Of these, 47 had the L452R mutation without the W152C mutation, typical in the B.1.617 variant. At week 25, this profile was found in 45.5 % of the samples and was the most frequent. CONCLUSION: According to our observations, variant B.1.617 has become predominant in our institution and most probably in our region. In the absence of the use of the Variants II Assay, they would have been considered wild.
URL: https://www.ncbi.nlm.nih.gov/pubmed/34332998
DOI: 10.1016/j.jviromet.2021.114248

ABSTRACT: Since January 2021, the diffusion of the most propagated SARS-CoV-2 variants in France (UK variant 20I/501Y.V1 (lineage B.1.1.7), 20H/H501Y.V2 (lineage B.1.351) and 20I/H501Y.V3 (lineage P.1)) were urgently screened, needing a surveillance with an RT-PCR screening assay. In this study, we evaluated one RT-PCR kit for this screening (ID SARS-CoV-2/UK/SA Variant Triplex(R), ID Solutions, Grabels, France) on 2207 nasopharyngeal samples that were positive for SARS-CoV-2. Using ID Solutions kit, 4.1% (92/2207) of samples were suspected to belonged to B.1.351 or P.1 variants. Next-generation sequencing that was performed on 67.4% (62/92) of these samples confirmed the presence of a B.1.351 variant in only 75.8% of the samples (47/62). Thirteen samples belonged to the UK variant (B.1.1.7), and two to A.27 with N501Y mutation. The thirteen with the UK variant presented one mutation in the S-gene, near the DeltaH69/DeltaV70 deletion (S71F or A67S), which impacted the detection of DeltaH69/DeltaV70 deletion. Using another screening kit (PKampVariantDetect SARS-CoV-2 RT-PCR combination 1 and 3((R)) PerkinElmer, Waltham, MA, USA) on the misidentified samples, we observed
that the two mutations, S71F or A67S, did not impact the detection of the UK variant. In conclusion, this study highlights the limitations of the screening strategy based on the detection of few mutations/deletions as well as it not being able to follow the virus evolution.

URL: https://www.ncbi.nlm.nih.gov/pubmed/34359323
DOI: 10.3390/diagnostics11071241


ABSTRACT: Molecular surveillance of SARS-CoV-2 variants was performed on a total of 2,406 samples from the capital city and nine provinces of Argentina, during 30 epidemiological weeks (EW) that covered the end of the first wave and the beginning of the ongoing second wave of the COVID-19 pandemic in the country (EW 44/2020 to EW 20/2021). The surveillance strategy was mainly based on Sanger sequencing of a Spike coding region that allows the simultaneous identification of signature mutations associated with worldwide circulating variants. In addition, whole SARS-CoV-2 genome sequences were obtained from 456 samples. The main variants found were Gamma, Lambda and Alpha, and to a lesser extent, Zeta and Epsilon. Whereas Gamma dominated in different regions of the country, both Gamma and Lambda prevailed in the most populated area, the metropolitan region of Buenos Aires (MABA), although showing a heterogeneous distribution along this region. This cost-effective surveillance protocol allowed for a rapid response in a limited access to resources scenario, added information on the expansion of the Lambda variant in South America and contributed to the implementation of public health measures to control the disease spread in Argentina.

Competing Interest Statement The authors have declared no competing interest. Funding Statement This work was supported by Proyecto IP COVID-19 N 08 and Focem COF 03/11 Covid-19. Author Declarations I confirm all relevant ethical guidelines have been followed, and any necessary IRB and/or ethics committee approvals have been obtained. Yes The details of the IRB/oversight body that provided approval or exemption for the research described are given below: All relevant ethical guidelines have been appropriately followed. The study was approved by the Ethics Committee of the Hospital de Ninos Ricardo Gutierrez, CABA, Argentina. All necessary patient/participant consent has been obtained and the appropriate institutional forms have been archived. Yes I understand that all clinical trials and any other prospective interventional studies must be registered with an ICMJE-approved registry, such as ClinicalTrials.gov. I confirm that any such study reported in the manuscript has been registered and the trial registration ID is provided (note: if posting a prospective study registered retrospectively, please provide a statement in the trial ID field explaining why the study was not registered in advance). Yes I have followed all appropriate research reporting guidelines and uploaded the relevant EQUATOR Network research reporting checklist(s) and other pertinent material as supplementary files, if applicable. Yes The sequences obtained in this study can be found in the online repository GISAID. URL: http://medrxiv.org/content/early/2021/07/22/2021.07.19.21260779.abstract DOI: 10.1101/2021.07.19.21260779


URL: https://www.ncbi.nlm.nih.gov/pubmed/34051887
DOI: 10.1016/S1473-3099(21)00287-5

**ABSTRACT:** As the global severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic expands, genomic epidemiology and whole genome sequencing are being used to investigate its transmission and evolution. Against the backdrop of the global emergence of "variants of concern" (VOCs) during December 2020 and an upsurge in a state in the western part of India since January 2021, whole genome sequencing and analysis of spike protein mutations using sequence and structural approaches were undertaken to identify possible new variants and gauge the fitness of the current circulating strains. Phylogenetic analysis revealed that newly identified lineages B.1.617.1 and B.1.617.2 were predominantly circulating. The signature mutations possessed by these strains were L452R, T478K, E484Q, D614G and P681R in the spike protein, including within the receptor-binding domain (RBD). Of these, the mutations at residue positions 452, 484 and 681 have been reported in other globally circulating lineages. The structural analysis of RBD mutations L452R, T478K and E484Q revealed that these may possibly result in increased ACE2 binding while P681R in the furin cleavage site could increase the rate of S1-S2 cleavage, resulting in better transmissibility. The two RBD mutations, L452R and E484Q, indicated decreased binding to select monoclonal antibodies (mAbs) and may affect their neutralization potential. Further in vitro/in vivo studies would help confirm the phenotypic changes of the mutant strains. Overall, the study revealed that the newly emerged variants were responsible for the second wave of COVID-19 in Maharashtra. Lineage B.1.617.2 has been designated as a VOC delta and B.1.617.1 as a variant of interest kappa, and they are being widely reported in the rest of the country as well as globally. Continuous monitoring of these and emerging variants in India is essential.

**URL:** https://www.ncbi.nlm.nih.gov/pubmed/34361977

**DOI:** 10.3390/microorganisms9071542


**ABSTRACT:** The COVID-19 pandemic has put healthcare infrastructures and our social and economic lives under unprecedented strain. Effective solutions are needed to end the pandemic while significantly lessening its further impact on mortality and social and economic life. Effective and widely-available vaccines have appropriately long been seen as the best way to end the pandemic. Indeed, the current availability of several effective vaccines are already making a significant progress towards achieving that goal. Nevertheless, concerns have risen due to new SARS-CoV-2 variants that harbor mutations against which current vaccines are less effective. Furthermore, some individuals are unwilling or unable to take the vaccine. As health officials across the globe scramble to vaccinate their populations to reach herd immunity, the challenges noted above indicate that COVID-19 therapeutics are still needed to work alongside the vaccines. Here we describe the impact that neutralizing antibodies have had on those with early or mild COVID-19, and what their approval for early management of COVID-19 means for other viral entry inhibitors that have a similar mechanism of action. Importantly, we also highlight studies that show that therapeutic strategies involving various viral entry inhibitors such as multivalent antibodies, recombinant ACE2 and miniproteins can be effective not only for pre-exposure prophylaxis, but also in protecting against SARS-CoV-2 antigenic drift and future zoonotic sarbecoviruses. Copyright © 2021, The Author(s).

**ABSTRACT:** Since summer 2020, SARS-CoV-2 strains at the origin of the COVID-19 pandemic have suddenly been replaced by new SARS-CoV-2 variants, some of which are highly transmissible and spread at a high rate. These variants include the Marseille-4 lineage (Nextclade 20A.EU2) in Europe, the 20I/501Y.V1 variant first detected in the UK, the 20H/501Y.V2 variant first detected in South Africa, and the 20I/501Y.V3 variant first detected in Brazil. These variants are characterized by multiple mutations in the viral spike protein that is targeted by neutralizing antibodies elicited in response to infection or vaccine immunization. The usual coronavirus mutation rate through genetic drift alone cannot account for such rapid changes. Recent reports of the occurrence of such mutations in immunocompromised patients who received remdesivir and/or convalescent plasma or monoclonal antibodies to treat prolonged SARS-CoV-2 infections led us to hypothesize that experimental therapies that fail to cure the patients from COVID-19 could favor the emergence of immune escape SARS-CoV-2 variants. We review here the data that support this hypothesis and urge physicians and clinical trial promoters to systematically monitor viral mutations by whole-genome sequencing for patients who are administered these treatments.

**URL:** https://www.ncbi.nlm.nih.gov/pubmed/34362060

**DOI:** 10.3390/jcm10153276


**URL:** https://www.ncbi.nlm.nih.gov/pubmed/34347959

**DOI:** 10.1056/NEJMsb2104756


**ABSTRACT:** Novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants are emerging worldwide. Here, we report the complete genome sequences of 13 severe acute SARS-CoV-2 strains belonging to lineage B.1.525 (variant eta).

**URL:** https://www.ncbi.nlm.nih.gov/pubmed/34351227

**DOI:** 10.1128/MRA.00618-21


**ABSTRACT:** The efficacy of COVID-19 mRNA vaccines is high, but breakthrough infections still occur. We compared the SARS-CoV-2 genomes of 76 breakthrough cases after full vaccination with BNT162b2 (Pfizer/BioNTech), mRNA-1273 (Moderna), or JNJ-78436735 (Janssen) to unvaccinated controls (February-April 2021) in metropolitan New York, including their phylogenetic relationship, distribution of variants, and full spike mutation profiles. Their median age was 48 years; seven required hospitalization and one died. Most breakthrough infections (57/76) occurred with B.1.1.7 (Alpha) or B.1.526 (Iota). Among the 7 hospitalized cases, 4 were infected with B.1.1.7, including 1 death. Both unmatched and matched statistical analyses considering age, sex, vaccine type, and study month as covariates supported the null hypothesis of equal variant distributions between vaccinated and unvaccinated in chi-squared and McNemar tests (p>0.1) highlighting a high vaccine efficacy against B.1.1.7 and B.1.526. There was no clear association among breakthroughs between type of vaccine received and variant. In the vaccinated group, spike mutations in the N-terminal domain and receptor-binding domain that have
been associated with immune evasion were overrepresented. The evolving dynamic of SARS-CoV-2 variants requires broad genomic analyses of breakthrough infections to provide real-life information on immune escape mediated by circulating variants and their spike mutations.

URL: https://www.ncbi.nlm.nih.gov/pubmed/34375308
DOI: 10.1172/JCI152702

URL: https://www.ncbi.nlm.nih.gov/pubmed/34330154

ABSTRACT: The current COVID-19 pandemic that is caused by SARS-CoV-2 has led all the people around the globe to implement preventive measures such as environmental cleaning using alcohol-based materials, and social distancing in order to prevent and minimize viral transmission via fomites. The role of environmental surface contamination in viral transmission in within hospital wards is still debatable, especially considering the spread of new variants of the virus in the world. The present comprehensive study aims to investigate environmental surface contamination in different wards of a hospital as well as the efficacy of two common disinfectants for virus inactivation, and tries to produce an estimate of plastic residue pollution as an environmental side effect of the pandemic. With regard to environmental surface contamination, 76 samples were taken from different wards of the hospital, from which 40 were positive. These samples were taken from contaminated environmental surfaces such as patient bed handles, the nursing station, toilet door handles, cell phones, patient toilet sinks, toilet bowls, and patient's pillows, which are regularly-touched surfaces and can pose a high risk for transmission of the virus. The number of positive samples also reveals that SARS-CoV-2 can survive on inanimate surfaces after disinfection by ethanol 70 % and sodium hypochlorite (0.001 %). The results correspond to the time that the VOC 202012/01 (lineage B.1.1.7) had emerged in the hospital and this should be considered that this variant could possibly have different traits, characteristics, and level of persistence in the environment. The plastic waste as an environmental side effect of the pandemic was also investigated and it was confirmed that the amount of plastic residue for a single (RT) PCR confirmatory test for COVID-19 diagnosis is 821.778 g of plastic residue/test. As a result, it is recommended that for improving plastic waste management programs, considering challenges such as minimizing plastic waste pollution, optimization of gas control technologies in incinerators, process redesign, reduction of single-use plastics and PPE, etc. Is of utmost importance.
URL: https://www.ncbi.nlm.nih.gov/pubmed/34333010
DOI: 10.1016/j.envres.2021.111809

ABSTRACT: Background: The degree of heterotypic immunity induced by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) strains is a major determinant of the spread of emerging variants and the success of vaccination campaigns, but remains incompletely understood. Method(s): We examined the immunogenicity of SARS-CoV-2 variant B.1.1.7 (Alpha) that arose in the United Kingdom and spread globally. We determined titres of spike glycoprotein-binding antibodies and authentic virus neutralising antibodies induced by B.1.1.7 infection to infer homotypic and heterotypic immunity. Result(s): Antibodies elicited by B.1.1.7 infection exhibited significantly reduced recognition and neutralisation of parental strains or of the South Africa variant B.1.351 (Beta) than of the infecting
variant. The drop in cross-reactivity was significantly more pronounced following B.1.1.7 than parental strain infection. Conclusion(s): The results indicate that heterotypic immunity induced by SARS-CoV-2 variants is asymmetric. Copyright © 2021, eLife Sciences Publications Ltd. All rights reserved.

25. Fort H. A very simple model to account for the rapid rise of the alpha variant of SARS-CoV-2 in several countries and the world. Virus Res. 2021;198531. DOI: 10.1016/j.virusres.2021.198531
ABSTRACT: Since its first detection in the UK in September 2020, a highly contagious version of the coronavirus, the alpha or British variant a.k.a. B.1.1.7 SARS-CoV-2 virus lineage, rapidly spread across several countries and became the dominant strain in the outbreak. Here it is shown that a very simple evolutionary model can fit the observed change in frequency of B.1.1.7 for several countries, regions of countries and the whole world with a single parameter, its relative fitness \( f \), which is almost universal \( f \approx 1.5 \). This is consistent with a 50% higher transmissibility than the local wild type and with the fact that the period in which this variant takes over has been in all the studied cases around 22 weeks.
URL: https://www.ncbi.nlm.nih.gov/pubmed/34363849
DOI: 10.1016/j.virusres.2021.198531

URL: https://www.ncbi.nlm.nih.gov/pubmed/34343259
DOI: 10.1093/cid/ciab676


ABSTRACT: OBJECTIVES: The emergence of new variants of concern (VOCs) of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) around the world significantly complicated the exit from Coronavirus disease 2019 (COVID-19) pandemic. The aim of this study was to evaluate the serum neutralizing activity of three cohorts. METHODS: BNT162b2-elicited serum (\( N = 103 \)), candidates as hyper-immune plasma donors (\( N = 90 \)) and patients infected with the SARS-CoV-2 P1 variant (\( N = 22 \)) were enrolled. Three strains of SARS-CoV-2 have been tested: 20A.EU1, B.1.1.7 (alpha) and P.1 (gamma). Neutralizing antibodies (NT-Abs) titers against SARS-CoV-2 were evaluated. RESULTS: B.1.1.7 and P.1 are less efficiently neutralized by convalescent wild-type infected sera if compared to 20A.EU1 strain (mean titer 1.6 and 6.7-fold lower respectively). BNT162b2 vaccine-elicited human sera show an equivalent neutralization potency on the B.1.1.7 but it is significantly lower for the P.1 variant (mean titer 3.3-fold lower). Convalescent P.1 patients are less protected from other SARS-CoV-2 strains with an important reduction of neutralizing antibodies against 20A.EU1 and B.1.1.7, about 12.2 and 10.9-fold, respectively. CONCLUSIONS: BNT162b2 vaccine confers immunity against all the tested VOCs, while previous SARS-CoV-2 infection may be less protective.
URL: https://www.ncbi.nlm.nih.gov/pubmed/34320390
DOI: 10.1016/j.jinf.2021.07.019

ABSTRACT: Since the beginning of the 2021 year, all the main six vaccines against COVID-19 have been used in mass vaccination companies around the world. Virus neutralization and epidemiological efficacy drop obtained for several vaccines against the B.1.1.7, B.1.351 P.1, and B.1.617 genotypes are of concern. There is a growing number of reports on mutations in receptor-binding domain (RBD) increasing the transmissibility of the virus and escaping the neutralizing effect of antibodies. The Sputnik V vaccine is currently approved for use in more than 66 countries but its activity against variants of concern (VOC) is not extensively studied yet. Virus-neutralizing activity (VNA) of sera obtained from people vaccinated with Sputnik V in relation to internationally relevant genetic lineages B.1.1.7, B.1.351, P.1, B.1.617.2, B.1.617.3 and Moscow endemic variants B.1.1.141 (T385I) and B.1.1.317 (S477N, A522S) with mutations in the RBD domain has been assessed. The data obtained indicate no significant differences in VNA against B.1.1.7, B.1.617.3 and local genetic lineages B.1.1.141 (T385I), B.1.1.317 (S477N, A522S) with RBD mutations. For the B.1.351, P.1, and B.1.617.2 statistically significant 3.1-, 2.8-, and 2.5-fold, respectively, VNA reduction was observed. Notably, this decrease is lower than that reported in publications for other vaccines. However, a direct comparative study is necessary for a conclusion. Thus, sera from "Sputnik V"-vaccinated retain neutralizing activity against VOC B.1.1.7, B.1.351, P.1, B.1.617.2, B.1.617.3 as well as local genetic lineages B.1.1.141 and B.1.1.317 circulating in Moscow.

URL: https://www.ncbi.nlm.nih.gov/pubmed/34358195
DOI: 10.3390/vaccines9070779


ABSTRACT: During the rapid worldwide spread of SARS-CoV-2, the viral genome has been undergoing numerous mutations, especially in the spike (S) glycoprotein gene that encode a type-I fusion protein, which plays an important role in the infectivity and transmissibility of the virus into the host cell. In this work, we studied the effect of S glycoprotein residue mutations on the binding affinity and mechanisms of SARS-CoV-2 using molecular dynamics simulations and sequence analysis. We quantitatively determined the degrees of binding affinity caused by different S glycoprotein mutations, and the result indicated that the 501Y.V1 variant yielded the highest enhancements in binding affinity (increased by 36.8%), followed by the N439K variant (increased by 29.5%) and the 501Y.V2 variant (increased by 19.6%). We further studied the structures, chemical bonds, binding free energies (enthalpy and entropy), and residue contribution decompositions of these variants to provide physical explanations for the changes in SARS-CoV-2 binding affinity caused by these residue mutations. This research identified the binding affinity differences of the SARS-CoV-2 variants and provides a basis for further surveillance, diagnosis, and evaluation of mutated viruses.

URL: https://www.ncbi.nlm.nih.gov/pubmed/34336146
DOI: 10.1016/j.csbj.2021.07.026


ABSTRACT: Wastewater surveillance has shown to be a valuable and efficient tool to obtain information about the trends of COVID-19 in the community. Since the recent emergence of new variants, associated with increased transmissibility and/or antibody escape (variants of concern), there is an urgent need for methods that enable specific and timely detection and quantification of the occurrence of these variants.
in the community. In this study, we demonstrate the use of RT-ddPCR on wastewater samples for specific detection of mutation N501Y. This assay enabled simultaneous enumeration of lineage B.1.351 (containing the 501Y mutation) and Wild Type (WT, containing 501N) SARS-CoV-2 RNA. Detection of N501Y was possible in samples with mixtures of WT with low proportions of B.1.351 (0.5%) and could accurately determine the proportion of N501Y and WT in mixtures of SARS-CoV-2 RNA. The application to raw sewage samples from the cities of Amsterdam and Utrecht demonstrated that this method can be applied to wastewater samples. The emergence of N501Y in Amsterdam and Utrecht wastewater aligned with the emergence of B.1.1.7 as causative agent of COVID-19 in the Netherlands, indicating that RT-ddPCR of wastewater samples can be used to monitor the emergence of the N501Y mutation in the community. It also indicates that RT-ddPCR could be used for sensitive and accurate monitoring of current (like K417N, K417T, E484K, L452R) or future mutations present in SARS-CoV-2 variants of concern. Monitoring these mutations can be used to obtain insight in the introduction and spread of VOC and support public health decision-making regarding measures to limit viral spread or allocation of testing or vaccination.

URL: https://www.ncbi.nlm.nih.gov/pubmed/34371414
DOI: 10.1016/j.scitotenv.2021.149456

ABSTRACT: Treatment options for COVID-19, a disease caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection, are currently severely limited. Therefore, antiviral drugs that efficiently reduce SARS-CoV-2 replication or alleviate COVID-19 symptoms are urgently needed. Inhaled glucocorticoids are currently being discussed in the context of treatment for COVID-19, partly based on a previous study that reported reduced recovery times in cases of mild COVID-19 after inhalative administration of the glucocorticoid budesonide. Given various reports that describe the potential antiviral activity of glucocorticoids against respiratory viruses, we aimed to analyze a potential antiviral activity of budesonide against SARS-CoV-2 and circulating variants of concern (VOC) B.1.1.7 (alpha) and B.1.351 (beta). We demonstrate a dose-dependent inhibition of SARS-CoV-2 that was comparable between all viral variants tested while cell viability remains unaffected. Our results are encouraging as they could indicate a multimodal mode of action of budesonide against SARS-CoV-2 and COVID-19, which could contribute to an improved clinical performance.

URL: https://www.ncbi.nlm.nih.gov/pubmed/34372616
DOI: 10.3390/v13071411

ABSTRACT: Escape variants can cause new waves of COVID-19 outbreaks and put vaccination strategies at risk. To prevent or delay the global spread of these waves, virus mobility needs to be minimised through screening and testing strategies, which should also cover vaccinated people. The costs of these strategies are minimal compared to the costs to health, society and the economy from another wave.

URL: https://www.ncbi.nlm.nih.gov/pubmed/34376870
DOI: 10.1007/s10272-021-0987-4

**ABSTRACT:** An outbreak caused by the SARS-CoV-2 Delta variant (B.1.617.2) spread from one inpatient in a secondary care hospital to three primary care facilities, resulting in 58 infections including 18 deaths in patients and 45 infections in healthcare workers (HCW). Only one of the deceased cases was fully vaccinated. Transmission occurred despite the use of personal protective equipment by the HCW, as advised in national guidelines, and a high two-dose COVID-19 vaccination coverage among permanent staff members in the COVID-19 cohort ward.


**DOI:** 10.2807/1560-7917.ES.2021.26.30.2100636


**ABSTRACT:** Fast evolving of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus has caused the spreading of COVID-19 disease rapidly around the globe. The mutation, especially in the gene encoding spike protein has helped the virus adapt and evade human immune system, as well as affect the efficacy of the immunizations and treatments. SARS-CoV-2 variant carrying D614G amino acid change at the spike protein is the most dominant strain in the pandemic. Therefore, efficient detection of the SARS-CoV-2 variants including D614G mutation is critical to control the COVID-19 pandemic. Herein, we report a dual synthetic mismatches CRISPR/Cas12a (dsmCRISPR) method to detect the SARS-CoV-2 D614G mutation with high sensitivity and specificity. By targeting SARS-CoV-2 D614G mutation, synthetic mismatch crRNAs were designed from -3 to +3 position around the mutation site. To improve the sensitivity and specificity, a synthetic mismatch primer with a 3'-terminal base complementary to the D614G point mutation and a mismatch next to 3'-terminal base was used to specifically amplify the D614G mutation site with higher annealing temperature. Using synthetic mismatch crRNA-(−1), a higher ratio (13.45) of the fluorescence between G614 and D614 was observed. When combined with mismatch primer to amplify D614G mutation, the fluorescence ratio of G614/D164 template detected was increased by 73.53% to 23.12. This method can detect the SARS-CoV-2 D614G mutation nucleic acid with high sensitivity, which was validated with synthetic SARS-CoV-2 D614G RNA. Therefore, the dsmCRISPR method has significant potential to serve as a sensitive and specific assay for SARS-CoV-2 D614G detection and could be further extended for the detection of other SARS-CoV-2 variants of interest.


**DOI:** 10.1016/j.virusres.2021.198530


**ABSTRACT:** How will the coronavirus disease 2019 (COVID-19) pandemic develop in the coming months and years? Based on an expert survey, we examine key aspects that are likely to influence the COVID-19 pandemic in Europe. The challenges and developments will strongly depend on the progress of national and global vaccination programs, the emergence and spread of variants of concern (VOCs), and public responses to non-pharmaceutical interventions (NPIs). In the short term, many people remain unvaccinated, VOCs continue to emerge and spread, and mobility and population mixing are expected to increase. Therefore, lifting restrictions too much and too early risk another damaging wave. This challenge remains despite the reduced opportunities for transmission given vaccination progress and
reduced indoor mixing in summer 2021. In autumn 2021, increased indoor activity might accelerate the spread again, whilst a necessary reintroduction of NPIs might be too slow. The incidence may strongly rise again, possibly filling intensive care units, if vaccination levels are not high enough. A moderate, adaptive level of NPIs will thus remain necessary. These epidemiological aspects combined with economic, social, and health-related consequences provide a more holistic perspective on the future of the COVID-19 pandemic.

URL: https://www.ncbi.nlm.nih.gov/pubmed/34345876
DOI: 10.1016/j.lanepe.2021.100185

ABSTRACT: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has infected at least 180 million people since its identification as the cause of the current COVID-19 pandemic. The rapid pace of vaccine development has resulted in multiple vaccines already in use worldwide. The contemporaneous emergence of SARS-CoV-2 ‘variants of concern’ (VOC) across diverse geographic locales underscores the need to monitor the efficacy of vaccines being administered globally. All WHO designated VOC carry spike (S) polymorphisms thought to enable escape from neutralizing antibodies. Here, we characterize the neutralizing activity of post-Sputnik V vaccination sera against the ensemble of S mutations present in alpha (B.1.1.7) and beta (B.1.351) VOC. Using de novo generated replication-competent vesicular stomatitis virus expressing various SARS-CoV-2-S in place of VSV-G (rcVSV-CoV2-S), coupled with a clonal 293T-ACE2 + TMPRSS2 + cell line optimized for highly efficient S-mediated infection, we determine that only 1 out of 12 post-vaccination serum samples shows effective neutralization (IC<sub>90</sub>) of rcVSV-CoV2-S: B.1.351 at full serum strength. The same set of sera efficiently neutralize S from B.1.1.7 and exhibit only moderately reduced activity against S carrying the E484K substitution alone. Taken together, our data suggest that control of some emergent SARS-CoV-2 variants may benefit from updated vaccines. Copyright © 2021, The Author(s).

ABSTRACT: Using numbers of SARS-CoV-2 variants detected in Japan as at 13 June 2021, relative instantaneous reproduction numbers (R<sub>RI</sub>) of the R.1, Alpha, and Delta variants with respect to other strains circulating in Japan were estimated at 1.25, 1.44, and 1.95. Depending on the assumed serial interval distributions, R<sub>RI</sub> varies from 1.20-1.32 for R.1, 1.34-1.58 for Alpha, and 1.70-2.30 for Delta. The frequency of Delta is expected to take over Alpha in Japan before 23 July 2021. Copyright © 2021 European Centre for Disease Prevention and Control (ECDC). All rights reserved.

ABSTRACT: Identifying the fundamental cause of transmissibility of multiple mutation strains and vaccine nullification is difficult in general and is a source of significant concern. The conformational variability of the mutation sites for B.1.617.2 (Delta), B.1.617.1 (kappa), B.1.427/429 (epsilon), P.1 (gamma), B.1.351 (beta), B.1.1.7 (alpha), S477N, and the wild-type strain has been assessed using a deep neural-network-based prediction program of conformational flexibility or rigidity in proteins (SSSSCPreds). We find that although the conformation of G614 is rigid, which is assigned as a left-handed (LH) alpha-helix-type one, that of D614 is flexible without the hydrogen bonding latch to T859. The rigidity of glycine, which stabilizes the local conformation more effectively than that of aspartic acid with the latch, thereby contributes to the reduction of S1 shedding, high expression, and increase in
The finding that the sequence flexibility/rigidity map pattern of B.1.1.7 is similar to that of the wild-type strain but is largely different from those of B.1.351 and P.1 correlates with the minor escape ability of B.1.1.7. The increased rigidity of the amino acid sequence YRYRLFR from the SSSCPreds data of B.1.427/429 near the L452R mutation site contributes to the 2-fold increased B.1.427/B.1.429 viral shedding in vivo and the increase in transmissibility relative to wild-type circulating strains in a similar manner to D614G. The concordance and rigidity ratios of multiple mutation strains such as B.1.617.2 against the wild-type one at the receptor-binding domain (RBD) and receptor-binding motif (RBM) regions provide a good indication of the transmissibility and neutralization escape ability except for binding affinity of mutation sites such as N501Y.

URL: https://www.ncbi.nlm.nih.gov/pubmed/34337269
DOI: 10.1021/acs.omega.1c03055

ABSTRACT: This review discusses the current testing methodologies for COVID-19 diagnosis and explores next-generation sequencing (NGS) technology for the detection of SARS-CoV-2 and monitoring phylogenetic evolution in the current COVID-19 pandemic. The review addresses the development, fundamentals, assay quality control and bioinformatics processing of the NGS data. This article provides a comprehensive review of the obstacles and opportunities facing the application of NGS technologies for the diagnosis, surveillance, and study of SARS-CoV-2 and other infectious diseases. Further, we have contemplated the opportunities and challenges inherent in the adoption of NGS technology as a diagnostic test with real-world examples of its utility in the fight against COVID-19. Copyright © 2021 by the authors. Licensee MDPI, Basel, Switzerland.

URL: https://www.ncbi.nlm.nih.gov/pubmed/34383043
DOI: 10.1001/jama.2021.13941

ABSTRACT: Introduction: The UK Obstetric Surveillance System (UKOSS) has reported on risk factors for admission to hospital amongst obstetric patients with SARS-CoV-2, however, it did not evaluate deprivation as a risk factor.<sup>1</sup> Deprivation is a recognised risk factor for mortality from COVID-19 amongst the general population.<sup>2</sup> We, therefore, investigated the demographics, including deprivation scores, of obstetric patients diagnosed with SARS-CoV-2 within our local health board. Method(s): Caldicott Guardian approval was obtained and requirement for ethical approval was waived by the local research ethics service. All pregnant or recently pregnant patients (within 6 weeks post-partum) within our health board area with a positive SARS-CoV-2 test between 16 March 2020 and 18 December 2020 were retrospectively identified from regional infection surveillance and local obstetric unit reports. Residential area deprivation was classified using the Scottish Index for Multiple Deprivation (SIMD), with quintile 1 representing the most deprived and quintile 5 representing the least deprived areas. R version 4.0.3 (R Foundation for Statistical Computing) was used to perform analyses. Result(s): Over the study period, 97 patients tested positive for SARS-CoV-2. Comparison between those in the lowest and highest SIMD quintiles is as shown below. Those from a black or ethnic minority background accounted for 31.9% of positive test results and 50% of admissions to critical care. [Formula
Discussion: In this cohort of obstetric patients, mothers from socioeconomically disadvantaged areas accounted for a higher proportion of SARS-CoV-2 positive cases (and hospital / critical care admissions) than those from more affluent areas. This is, to our knowledge, the first study to investigate this association in obstetric patients. The relationship demonstrated between ethnicity, deprivation and SARS-CoV-2 requires further investigation and may have implications for future resource allocation and service planning. Copyright © 2021

ABSTRACT: Cases of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) acquisition after vaccination with BNT162b2 have been described, but the risk of secondary transmission from fully vaccinated individuals remains ill defined. Herein we report a confirmed transmission of SARS-CoV-2 alpha variant (B.1.1.7) from a symptomatic immunocompetent woman 4 weeks after her second dose of BNT162b2, despite antispire seroconversion.
URL: https://www.ncbi.nlm.nih.gov/pubmed/34377731
DOI: 10.1093/ofid/ofab369

ABSTRACT: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the causative agent of the current coronavirus disease 2019 (COVID-19) pandemic. It is known that the receptor-binding domain (RBD) of the spike protein of SARS-CoV-2 interacts with the human angiotensin-converting enzyme 2 (ACE2) receptor, initiating the entry of SARS-CoV-2. Since its emergence, a number of SARS-CoV-2 variants have been reported, and the variants that show high infectivity are classified as the variants of concern according to the US CDC. In this study, we performed both all-atom steered molecular dynamics (SMD) simulations and microscale thermophoresis (MST) experiments to characterize the binding interactions between ACE2 and RBD of all current variants of concern (Alpha, Beta, Gamma, and Delta) and two variants of interest (Epsilon and Kappa). We report that the RBD of the Alpha (N501Y) variant requires the highest amount of force initially to be detached from ACE2 due to the N501Y mutation in addition to the role of N90-glycan, followed by Beta/Gamma (K417N/T, E484K, and N501Y) or Delta (L452R and T478K) variant. Among all variants investigated in this work, the RBD of the Epsilon (L452R) variant is relatively easily detached from ACE2. Our results combined SMD simulations and MST experiments indicate what makes each variant more contagious in terms of RBD and ACE2 interactions. This study could help develop new drugs to inhibit SARS-CoV-2 entry effectively. Abstract Figure:
URL: https://www.ncbi.nlm.nih.gov/pubmed/34341794
DOI: 10.1101/2021.07.23.453598

DOI: 10.1016/j.nmni.2021.100929
ABSTRACT: Many proactive steps have been taken worldwide to fight against the SARS-CoV-2 pandemic and to prevent COVID-19 spread with realistic approaches. Recently, a novel variant B.1.617.2 has been identified in India, which is rapidly transmitting to other countries, challenging current therapeutics, wide vaccination and future research in COIVD-19.
URL: https://www.ncbi.nlm.nih.gov/pubmed/34336227
DOI: 10.1016/j.nmni.2021.100929

**ABSTRACT:** SARS-CoV-2 escape mutations (EM) have been detected and are spreading. Vaccines may need adjustment to respond to these or future mutations. We designed a population level model integrating both waning immunity and EM. We also designed a set of criteria for elaborating and fitting this model to cross-neutralization and other data with a goal of minimizing vaccine decision errors. We formulated four related models. These differ regarding which strains can drift to escape immunity in the host when that immunity was elicited by different strains. Across changing waning and escape mutation parameter values, these model variations led to patterns where: 1) EM are rare in the first epidemic, 2) rebound outbreaks after the first outbreak are accelerated by increasing waning and by increasing drifting, 3) the long term endemic level of infection is determined mostly by waning rates with small effects of the drifting parameter, 4) EM caused loss of vaccine effectiveness, and under some conditions: vaccines induced EM that caused higher levels of infection with vaccines than without them. The differences and similarities across the four models suggest paths for developing models specifying the epitopes where EM act. This model provides a base on which to construct epitope specific evolutionary models using new high-throughput assay data from population samples to guide vaccine decisions.

URL: https://www.ncbi.nlm.nih.gov/pubmed/34375814
DOI: 10.1016/j.epidem.2021.100484


URL: https://www.ncbi.nlm.nih.gov/pubmed/33992685
DOI: 10.1016/j.jinf.2021.05.008


**ABSTRACT:** A breakthrough infection occurred in a fully Comirnaty (BNT162b2) vaccinated healthcare worker with high levels of neutralising antibodies with the SARS-CoV-2 B.1.351 (Beta) variant in February 2021. The infection was subsequently transmitted to their unvaccinated spouse. Sequencing revealed an identical virus in both spouses, with a match of all nine single nucleotide polymorphisms typical for B.1.351. To the best of our knowledge, no transmission of any variant of SARS-CoV-2 from a fully vaccinated person has been described before.

URL: https://www.ncbi.nlm.nih.gov/pubmed/34328074


**ABSTRACT:** Emerging variants of concern for the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) can transmit more efficiently and partially evade protective immune responses, thus necessitating continued refinement of antibody therapeutics and immunogen design. Here we elucidate the structural basis and mode of action for two potent SARS-CoV-2 Spike (S) neutralizing monoclonal antibodies CV3-1 and CV3-25 that remained effective against emerging variants of concern in vitro and in vivo. CV3-1 bound to the (485-GFN-487) loop within the receptor-binding domain (RBD) in the "RBD-up" position and triggered potent shedding of the S1 subunit. In contrast, CV3-25 inhibited membrane fusion by binding to an epitope in the stem helix region of the S2 subunit that is highly conserved among
beta-coronaviruses. Thus, vaccine immunogen designs that incorporate the conserved regions in RBD and stem helix region are candidates to elicit pan-coronavirus protective immune responses.

URL: https://www.ncbi.nlm.nih.gov/pubmed/34373853
DOI: 10.1101/2021.08.02.454546

URL: https://www.ncbi.nlm.nih.gov/pubmed/34353390
DOI: 10.1017/ice.2021.364

URL: https://www.ncbi.nlm.nih.gov/pubmed/33979486
DOI: 10.1056/NEJMc2106083

52. Liu Y, Rocklov J. The reproductive number of the Delta variant of SARS-CoV-2 is far higher compared to the ancestral SARS-CoV-2 virus. J Travel Med. 2021;09:09. DOI: 10.1093/nterm/taab124
ABSTRACT: The Delta variant is now replacing all other SARS-CoV-2 variants. We found a mean R0 of 5.08 which is much higher than the R0 of the ancestral strain of 2.79. Rapidly ramping up vaccine coverage rates while enhancing public health and social measures is now even more urgent and important.
URL: https://www.ncbi.nlm.nih.gov/pubmed/34369565
DOI: 10.1093/nterm/taab124

ABSTRACT: Background: Solid-organ transplant (SOT) recipients are at a high risk of severe COVID-19, and are priority for vaccination. Here, we describe three cases of severe COVID-19 caused by SARS-CoV-2 B.1.1.7 lineage in vaccinated SOT recipients. Method(s): Three SOT patients were hospitalized in the Policlinico Hospital of Bari (southern Italy) and underwent nasopharyngeal swabs for molecular detection of SARS-CoV-2 genes and spike protein mutations by real-time PCR. One sample was subjected to whole-genome sequencing. Result(s): One patient was a heart transplant recipient and two were kidney transplant recipients. All were hospitalized with severe COVID-19 between March and May 2021. Two patients were fully vaccinated and one had received only one dose of the BNT162b2 mRNA vaccine. All the patients showed a high viral load at diagnosis, and molecular typing revealed the presence of B.1.1.7 lineage SARS-CoV-2. In all three cases, prolonged viral shedding was reported. Conclusion(s): The three cases pose concern about the role of the B.1.1.7 lineage in severe COVID-19 and about the efficacy of COVID-19 vaccination in immunocompromised patients. Protecting immunocompromised patients from COVID-19 is a challenge. SOT recipients show a suboptimal response to standard vaccination, and thus, an additive booster or a combined vaccination strategy with mRNA, protein/subunit, and vector-based vaccines may be necessary. This population should continue to practice strict COVID-19 precautions post-vaccination, until new strategies for protection are available. Copyright © 2021 by the authors.
ABSTRACT: BACKGROUND: The emergence of COVID-19 pandemic resulted in an urgent need for the development of therapeutic interventions. Of which, neutralizing antibodies play a crucial role in the prevention and resolution of viral infection. METHODS: We generated antibody libraries from 18 different COVID-19 recovered patients and screened neutralizing antibodies to SARS-CoV-2 and its mutants. After 3 rounds of panning, 456 positive phage clones were obtained with high affinity to RBD (receptor binding domain). Clones were then reconstituted into whole human IgG for epitope binning assay and all 19 IgG were classified into 6 different epitope groups or Bins. RESULTS: Although all antibodies were found to bind RBD, the antibodies in Bin2 had superior inhibitory ability of the interaction between spike protein and angiotensin converting enzyme 2 receptor (ACE2). Most importantly, the antibodies from Bin2 showed stronger binding affinity or ability to mutant RBDs (N501Y, W463R, R408I, N354D, V367F and N354D/D364Y) derived from different SARS-CoV-2 strains as well, suggesting the great potential of these antibodies in preventing infection of SARS-CoV-2 and its mutations. Furthermore, such neutralizing antibodies strongly restricted the binding of RBD to hACE2 overexpressed 293T cells. Consistently, these antibodies effectively neutralized wildtype and more transmissible mutant pseudovirus entry into hACE2 overexpressed 293T cells. In Vero-E6 cells, one of these antibodies can even block the entry of live SARS-CoV-2 into cells at 12.5 nM. DISCUSSION: These results indicate that the neutralizing human antibodies from the patient-derived antibody libraries have the potential to fight SARS-CoV-2 and its mutants in this global pandemic. This article is protected by copyright. All rights reserved.
URL: https://www.ncbi.nlm.nih.gov/pubmed/34379353
DOI: 10.1002/biot.202100207

ABSTRACT: Although traditional models of epidemic spreading focus on the number of infected, susceptible and recovered individuals, a lot of attention has been devoted to integrate epidemic models with population genetics. Here we develop an individual-based model for epidemic spreading on networks in which viruses are explicitly represented by finite chains of nucleotides that can mutate inside the host. Under the hypothesis of neutral evolution we compute analytically the average pairwise genetic distance between all infecting viruses over time. We also derive a mean-field version of this equation that can be added directly to compartmental models such as SIR or SEIR to estimate the genetic evolution. We compare our results with the inferred genetic evolution of SARS-CoV-2 at the beginning of the epidemic in China and found good agreement with the analytical solution of our model. Finally, using genetic distance as a proxy for different strains, we use numerical simulations to show that the lower the connectivity between communities, e.g., cities, the higher the probability of reinfection.
URL: https://www.ncbi.nlm.nih.gov/pubmed/34324605
DOI: 10.1371/journal.pone.0255438

DOI: 10.3389/fimmu.2021.701501
ABSTRACT: Coronavirus 19 Disease (COVID-19) originating in the province of Wuhan, China in 2019, is caused by the severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2), whose infection in humans causes mild or severe clinical manifestations that mainly affect the respiratory system. So far, the COVID-19 has caused more than 2 million deaths worldwide. SARS-CoV-2 contains the Spike (S) glycoprotein on its surface, which is the main target for current vaccine development because
antibodies directed against this protein can neutralize the infection. Companies and academic institutions have developed vaccines based on the S glycoprotein, as well as its antigenic domains and epitopes, which have been proven effective in generating neutralizing antibodies. However, the emergence of new SARS-CoV-2 variants could affect the effectiveness of vaccines. Here, we review the different types of vaccines designed and developed against SARS-CoV-2, placing emphasis on whether they are based on the complete S glycoprotein, its antigenic domains such as the receptor-binding domain (RBD) or short epitopes within the S glycoprotein. We also review and discuss the possible effectiveness of these vaccines against emerging SARS-CoV-2 variants.

URL: https://www.ncbi.nlm.nih.gov/pubmed/34322129
DOI: 10.3389/fimmu.2021.701501


ABSTRACT: In December 2020, UK authorities warned of the rapid spread of a new SARS-CoV-2 variant, belonging to the B.1.1.7 lineage, known as the Alpha variant. This variant is characterized by 17 mutations and 3 deletions. The deletion 69-70 in the spike protein can be detected by commercial platforms, allowing its real-time spread to be known. From the last days of December 2020 and over 4 months, all respiratory samples with a positive result for SARS-CoV-2 from patients treated in primary care and the emergency department were screened to detect this variant based on the strategy S gene target failure (SGTF). The first cases were detected during week 53 (2020) and reached >90% of all cases during weeks 15-16 (2021). During this period, the B.1.1.7/SGTF variant spread at a rapid and constant replacement rate of around 30-36%. The probability of intensive care unit admission was twice higher among patients infected by the B.1.1.7/SGTF variant, but there were no differences in death rate. During the peak of the third pandemic wave, this variant was not the most prevalent, and it became dominant when this wave was declining. Our results confirm that the B.1.1.7/SGTF variant displaced other SARS-CoV-2 variants in our healthcare area in 4 months. This displacement has led to an increase in the burden of disease.

URL: https://www.ncbi.nlm.nih.gov/pubmed/34361951
DOI: 10.3390/microorganisms9071517


DOI: 10.20944/preprints202108.0058.v1


URL: https://www.ncbi.nlm.nih.gov/pubmed/34329486
DOI: 10.1002/jmv.27247


URL: https://www.ncbi.nlm.nih.gov/pubmed/34321116
DOI: 10.1017/cjn.2021.183

ABSTRACT: Background: Since its emergence in Autumn 2020, the SARS-CoV-2 Variant of Concern (VOC) B.1.1.7 (WHO label Alpha) rapidly became the dominant lineage across much of Europe. Simultaneously, several other VOCs were identified globally. Unlike B.1.1.7, some of these VOCs possess mutations thought to confer partial immune escape. Understanding when and how these additional VOCs pose a threat in settings where B.1.1.7 is currently dominant is vital. Method(s): We examine trends in the prevalence of non-B.1.1.7 lineages in London and other English regions using passive-case detection PCR data, cross-sectional community infection surveys, genomic surveillance, and wastewater monitoring. The study period spans from 31st January 2021 to 15th May 2021. Finding(s): Across data sources, the percentage of non-B.1.1.7 variants has been increasing since late March 2021. This increase was initially driven by a variety of lineages with immune escape. From mid-April, B.1.617.2 (WHO label Delta) spread rapidly, becoming the dominant variant in England by late May. Interpretation(s): The outcome of competition between variants depends on a wide range of factors such as intrinsic transmissibility, evasion of prior immunity, demographic specificities and interactions with non-pharmaceutical interventions. The presence and rise of non-B.1.1.7 variants in March likely was driven by importations and some community transmission. There was competition between non-B.1.17 variants which resulted in B.1.617.2 becoming dominant in April and May with considerable community transmission. Our results underscore that early detection of new variants requires a diverse array of data sources in community surveillance. Continued real-time information on the highly dynamic composition and trajectory of different SARS-CoV-2 lineages is essential to future control efforts Funding: National Institute for Health Research, Medicines and Healthcare products Regulatory Agency, DeepMind, EPSRC, EA Funds programme, Open Philanthropy, Academy of Medical Sciences Bill, Melinda Gates Foundation, Imperial College Healthcare NHS Trust, The Novo Nordisk Foundation, MRC Centre for Global Infectious Disease Analysis, Community Jameel, Cancer Research UK, Imperial College COVID-19 Research Fund, Medical Research Council, Wellcome Sanger Institute. Copyright © 2021 The Authors

URL: https://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=emexb&AN=20138287


ABSTRACT: With increasing global cases and mortality rates due to COVID-19 infection, finding effective therapeutic interventions has become a top priority. Marine resources are not explored much and to be taken into consideration for exploring antiviral potential. Chitosan (carbohydrate polymer) is one such bioactive glycan found ubiquitously in marine organisms. The presence of reactive amine/hydroxyl groups, with low toxicity/allergenicity, compels us to explore it against SARS-CoV-2. We have screened a library of chitosan derivatives by site-specific docking at not only spike protein Receptor Binding Domain (RBD) of wild type SARS-CoV-2 but also on RBD of B.1.1.7 (UK) and P.1 (Brazil) SARS-CoV-2 variants. The obtained result was very interesting and ranks N-benzyl-O-acetyl-chitosan, Imino-chitosan, Sulfated-chitosan oligosaccharides derivatives as a potent antiviral candidate due to its high binding affinity of the ligands (~6.0 to ~6.6 kcal/mol) with SARS-CoV-2 spike protein RBD and they critically interacting with amino acid residues Tyr 449, Asn 501, Tyr 501, Gln 493, Gln 498 and some other site-specific residues associated with higher transmissibility and severe infection. Further ADMET analysis was done and found significant for exploration of the future therapeutic potential of these three ligands. The obtained results are highly encouraging in support for consideration and exploration in further clinical studies of these chitosan derivatives as anti-SARS-CoV-2 therapeutics.

**ABSTRACT:** The B.1.1.7 SARS-CoV-2 strain that has emerged in the UK in early December presents seven mutations and three deletions on S-protein structure that could lead to a more infective strain. The P681H mutation in the "PRRAR" furin cleavage site might affect the binding affinity to furin enzyme and hence its infectivity. Therefore, in this study, various structural bioinformatics approaches were used to model the S-protein structure with the B.1.1.7 variant amino acid substitutions and deletions. In addition to modelling the binding of furin to the cleavage site of the wild-type and the B.1.1.7 variant. Conclusively the B.1.1.7 variant resulted in dynamic stability, conformational changes and variations in binding energies in the S-protein structure, resulting in a more favourable binding of furin enzyme to the SARS-CoV-2 S-protein.

**URL:** https://www.ncbi.nlm.nih.gov/pubmed/34314772
**DOI:** 10.1016/j.virusres.2021.198522


**ABSTRACT:** At present, global vaccination for the SARS-CoV2 virus 2019 (COVID-19) is 95% effective. Generally, viral infections are arduous to cure due to the mutating nature of viral genomes, with the consequent quick development of resistance, posing significant fatalities or hazards. The novel corona viral strains are increasingly lethal than earlier variants, as those evolve faster than imagined. Despite the emergence of several present innovative treatment options, the vaccines, and available drugs, the latter still are the needs of the time. Therefore, repurposing the approved pharmaceutical drugs of a well-known safety profile would be ascertained to provide faster antiviral approaches for the newer strains of COVID-19. Recently, a combination of remdesivir, which has a competitively inhibitory effect on the nucleotide uptake in the virus, and the merimepodibs, an inhibitor of the enzyme inosine monophosphate dehydrogenase, which has a role in the synthesis of nucleotides of guanine bases, is in use in phase 2 clinical trials. However, new investigations suggest that using remdesivir, there is no statistically significant difference with uncertain clinical importance for moderate COVID-19 patients. Herein, an intellectual selection of approved drugs based on the safety profile is described, to target any essential enzymes that are required for the virus-receptor contact, fusion, and/or different stages of the life cycle of this virus, should help to screen drugs against newer strains of COVID-19. Graphical abstract.

**URL:** https://www.ncbi.nlm.nih.gov/pubmed/34378108
**DOI:** 10.1208/s12249-021-02089-5


**ABSTRACT:** Antibodies elicited by infection accumulate somatic mutations in germinal centers that can increase affinity for cognate antigens. We analyzed 6 independent groups of clonally related severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) Spike receptor-binding domain (RBD)-specific antibodies from 5 individuals shortly after infection and later in convalescence to determine the impact of maturation over months. In addition to increased affinity and neutralization potency, antibody evolution changed the mutational pathways for the acquisition of viral resistance and restricted...
neutralization escape options. For some antibodies, maturation imposed a requirement for multiple substitutions to enable escape. For certain antibodies, affinity maturation enabled the neutralization of circulating SARS-CoV-2 variants of concern and heterologous sarbecoviruses. Antibody-antigen structures revealed that these properties resulted from substitutions that allowed additional variability at the interface with the RBD. These findings suggest that increasing antibody diversity through prolonged or repeated antigen exposure may improve protection against diversifying SARS-CoV-2 populations, and perhaps against other pandemic threat coronaviruses.

URL: https://www.ncbi.nlm.nih.gov/pubmed/34331873
DOI: 10.1016/j.immuni.2021.07.008

URL: https://www.ncbi.nlm.nih.gov/pubmed/34339484

ABSTRACT: The spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants, such as B.1.1.7 and B.1.351, has become a crucial issue worldwide. Therefore, we began testing all patients with COVID-19 for the N501Y and E484K mutations by using polymerase chain reaction (PCR)-based methods. Nasopharyngeal swab samples from 108 patients who visited our hospital between February and April 2021 were analyzed. The samples were analyzed using reverse transcription-PCR with melting curve analysis to detect the N501Y and E484K mutations. A part of the samples was also subjected to whole-genome sequencing (WGS). Clinical parameters such as mortality and admission to the intensive care unit were analyzed to examine the association between increased disease severity and the E484K mutation. The ratio of cases showing the 501N + 484K mutation rapidly increased from 8% in February to 46% in March. WGS revealed that the viruses with 501N + 484K mutation are R.1 lineage variants. Evidence of increased disease severity related to the R.1 variants was not found. We found that the R.1 lineage variants rapidly prevailed in Tokyo in March 2021, which suggests the increased transmissibility of R.1 variants, while they showed no increased severity. Copyright © 2021 Wiley Periodicals LLC

URL: https://www.ncbi.nlm.nih.gov/pubmed/34353385
DOI: 10.1017/ice.2021.363

ABSTRACT: The pandemic generated by SARS-Cov-2 has caused a large number of cases and deaths in the world, but South America has been one of the continents most hardly hit. The appearance of new variants causes concern because of the possibility that they may evade the protection generated by vaccination campaigns, because of their greater capacity to be transmitted or due to their greater virulence. We analyzed the circulating variants in Peru after improving our Genomic Surveillance program. The results indicate a steep increase of the lambda lineage (C.37) until becoming predominant between January and April 2021, despite the co-circulation of other variants of concern or interest. Lambda lineage deserves close monitoring and could probably become a variant of concern in the near future. This article is protected by copyright. All rights reserved.
URL: https://www.ncbi.nlm.nih.gov/pubmed/34370324

**ABSTRACT:** Airborne transmission, a term combining both large droplet and aerosol transmission, is thought to be the main transmission route of SARS-CoV-2. Here we investigated the relative efficiency of aerosol transmission of two variants of SARS-CoV-2, B.1.1.7 (alpha) and lineage A, in the Syrian hamster. A novel transmission caging setup was designed and validated, which allowed the assessment of transmission efficiency at various distances. At 2 meters distance, only particles <5 microm traversed between cages. In this setup, aerosol transmission was confirmed in 8 out of 8 (N = 4 for each variant) sentinels after 24 hours of exposure as demonstrated by respiratory shedding and seroconversion. Successful transmission occurred even when exposure time was limited to one hour, highlighting the efficiency of this transmission route. Interestingly, the B.1.1.7 variant outcompeted the lineage A variant in an airborne transmission chain after mixed infection of donors. Combined, this data indicates that the infectious dose of B.1.1.7 required for successful transmission may be lower than that of lineage A virus. The experimental proof for true aerosol transmission and the increase in the aerosol transmission potential of B.1.1.7 underscore the continuous need for assessment of novel variants and the development or preemptive transmission mitigation strategies.

**URL:** https://www.ncbi.nlm.nih.gov/pubmed/34341792

**DOI:** 10.1101/2021.07.26.453518


**ABSTRACT:** Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the etiological agent of the coronavirus disease 2019 (COVID-19) pandemic, which has been a topic of major concern for global human health. The challenge to restrain the COVID-19 pandemic is further compounded by the emergence of several SARS-CoV-2 variants viz. B.1.1.7 (Alpha), B.1.351 (Beta), P1 (Gamma) and B.1.617.2 (Delta), which show increased transmissibility and resistance towards vaccines and therapies. Importantly, there is convincing evidence of increased susceptibility to SARS-CoV-2 infection among individuals with dysregulated immune response and comorbidities. Herein, we provide a comprehensive perspective regarding vulnerability of SARS-CoV-2 infection in patients with underlying medical comorbidities. We discuss ongoing vaccine (mRNA, protein-based, viral vector-based, etc.) and therapeutic (monoclonal antibodies, small molecules, plasma therapy, etc.) modalities designed to curb the COVID-19 pandemic. We also discuss in detail, the challenges posed by different SARS-CoV-2 variants of concern (VOC) identified across the globe and their effects on therapeutic and prophylactic interventions.

**URL:** https://www.ncbi.nlm.nih.gov/pubmed/34356617

**DOI:** 10.3390/biom11070993


**ABSTRACT:** We report the emergence of a novel lineage of SARS-CoV-2 in South America, termed C.37. It presents seven nonsynonymous mutations in the Spike gene (Δ247-253, G75V, T76I, L452Q, F490S, T859N) and a deletion in the ORF1a gene (Δ3675-3677) also found in variants of concern (VOCs) Alpha, Beta, and Gamma. Initially reported in Lima, Peru, in late December 2020, it now accounts for 97% of Peruvian public genomes in April 2021. It is expanding in Chile and Argentina, and there is evidence of onward transmission in Colombia, Ecuador, Mexico, the USA, Germany, and Israel. On June 15, 2021, the World Health Organization designated C.37 as Variant of Interest (V0I) Lambda.
Statement
The authors have declared no competing interest.

Funding Statement
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Author Declarations
I confirm all relevant ethical guidelines have been followed, and any necessary IRB and/or ethics committee approvals have been obtained. Yes

The details of the IRB/oversight body that provided approval or exemption for the research described are given below: The Institutional Review Board of Universidad Peruana Cayetano Heredia approved the project in June 2020 (E051-12-20). All necessary patient/participant consent has been obtained and the appropriate institutional forms have been archived. Yes

I understand that all clinical trials and any other prospective interventional studies must be registered with an ICMJE-approved registry, such as ClinicalTrials.gov. I confirm that any such study reported in the manuscript has been registered and the trial registration ID is provided (note: if posting a prospective study registered retrospectively, please provide a statement in the trial ID field explaining why the study was not registered in advance). Yes

I have followed all appropriate research reporting guidelines and uploaded the relevant EQUATOR Network research reporting checklist(s) and other pertinent material as supplementary files, if applicable. Yes

All analyzed sequences were publicly available in GISAID at the time of submission. Raw Illumina reads from 350 Peruvian genomes sequenced at UPCH are available at NCBI BioProject PRJNA667090.

URL: http://medrxiv.org/content/early/2021/07/03/2021.06.26.21259487.abs tract
DOI: 10.1101/2021.06.26.21259487


ABSTRACT: SARS-CoV-2 mutations appeared recently and can lead to conformational changes in the spike protein and probably induce modifications in antigenicity. We assessed the neutralizing capacity of antibodies to prevent cell infection, using a live virus neutralization test with different strains [19A (initial one), 20B (B.1.1.241 lineage), 20I/501Y.V1 (B.1.1.7 lineage), and 20H/501Y.V2 (B.1.351 lineage)] in serum samples collected from different populations: two-dose vaccinated COVID-19-naive healthcare workers (HCWs; Pfizer-BioNTech BNT161b2), 6-months post mild COVID-19 HCWs, and critical COVID-19 patients. No significant difference was observed between the 20B and 19A isolates for HCWs with mild COVID-19 and critical patients. However, a significant decrease in neutralization ability was found for 20I/501Y.V1 in comparison with 19A isolate for critical patients and HCWs 6-months post infection. Concerning 20H/501Y.V2, all populations had a significant reduction in neutralizing antibody titers in comparison with the 19A isolate. Interestingly, a significant difference in neutralization capacity was observed for vaccinated HCWs between the two variants but not in the convalescent groups.

URL: https://www.ncbi.nlm.nih.gov/pubmed/34176436
DOI: 10.1080/22221751.2021.1945423


ABSTRACT: The study demonstrated that the breakthrough cases and the COVID-19 recovered individuals with one or two doses of Covishield vaccine had relatively higher neutralizing responses against the Delta variant in comparison to the participants who were administered either one or two doses of Covishield.

URL: https://www.ncbi.nlm.nih.gov/pubmed/34343316
DOI: 10.1093/jtm/taab119

ABSTRACT: Three COVID-19 waves in Japan have been characterized by the presence of distinct PANGO lineages (B.1.1.162, B.1.1.284, and B.1.1.214). Recently, in addition to the B.1.1.7 lineage, which shows 25% abundance, an R.1 lineage carrying the E484K mutation in the spike protein was found to show up to 40% predominance. E484K could be a pivotal amino acid substitution with the potential to mediate immune escape; thus, more attention should be paid to such potential variants of concern to avoid the emergence of mutants of concern. Such comprehensive real-time genome surveillance has become essential for the containment of COVID-19 clusters.

URL: https://www.ncbi.nlm.nih.gov/pubmed/34352360
DOI: 10.1016/j.meegid.2021.105013


ABSTRACT: We report that there is a recent global expansion of numerous independent SARS-CoV-2 variants with mutation L452R in the receptor-binding domain (RBD) of the Spike protein. The massive emergence of L452R variants was first linked to lineage B.1.427/B.1.429 (clade 21C) that has been spreading in California since November-December 2020, originally named CAL.20C and currently variant of interest Epsilon. By PCR amplification and Sanger sequencing of a 541 base fragments coding for amino acids 414-583 of RBD from a collection of clinical specimens, we identified a separate L452R variant that also recently emerged in California but derives from the lineage B.1.232, clade 20A (named CAL.20A). Notably, CAL.20A caused an infection in gorillas in the San Diego Zoo, reported in January 2021. Unlike the Epsilon variant that carries two additional mutations in the N-terminal domain of Spike protein, L452R is the only mutation found in the Spike proteins of CAL.20A. Based on genome-wide phylogenetic analysis, emergence of both viral variants was specifically triggered by acquisition of L452R, suggesting a strong positive selection for this mutation. Global analysis revealed that L452R is nearly omnipresent in a dozen independently emerged lineages, including the most recent variants of concern/interest Delta, Kappa, Epsilon and Iota, with the Lambda variant carrying L452Q. L452 is in immediate proximity to the ACE2 interaction interface of RBD. It was reported that the L452R mutation is associated with immune escape and could result in a stronger cell attachment of the virus, with both factors likely increasing viral transmissibility, infectivity and pathogenicity.

URL: https://www.ncbi.nlm.nih.gov/pubmed/34379531
DOI: 10.1128/JCM.00921-21


ABSTRACT: A 72-year-old immunocompromised man infected with severe acute respiratory syndrome coronavirus 2 received bamlanivimab monotherapy. Viral evolution was monitored in nasopharyngeal and blood samples by melting curve analysis of single-nucleotide polymorphisms and whole-genome sequencing. Rapid emergence of spike receptor binding domain mutations was found, associated with a compartmentalization of viral populations.

URL: https://www.ncbi.nlm.nih.gov/pubmed/34352197
DOI: 10.3201/eid2710.211509

ABSTRACT: Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) emerged in late December 2019 in Wuhan, China. More than 83 million people have been infected, and more than 1.8 million people have died, as reported to the World Health Organization on the 3rd of January, 2021. Analysis of genetic variations is critical for understanding the spreading pattern of SARS-CoV-2 across several countries. This review aimed to gather information about the prominent mutations of SARS-CoV-2 by analyzing the origin, viral pathogenesis, and mutation rate. Moreover, we concluded their potential impacts on SARS-CoV-2 therapeutics. Mutations in the spike protein (D614G, N501Y, E484K, A222V, S477N, and G485R), ORF1ab (P323L, N628N, Y455Y, A97V, and F106F), nucleocapsid protein (R203K and G204R), ORF8 (L845), and ORF3a (Q57H and G251V) were examined in this review by analyzing relevant articles from the beginning of the current pandemic to the most recent date. A detailed analysis of articles demonstrates that D614G is the major variation distributed globally, and its frequency increased rapidly from early in March, followed by several other variations in either spike or different proteins. In addition, it was seen that the currently circulating N501Y and E484K variants revealed a public concern regarding vaccines’ efficacy. Investigation of variations of SARS-CoV-2 would lead to understanding their potential mechanism of action against SARS-CoV-2, thereby suggesting suitable therapeutics. Several mechanisms were suggested to have a role in SARS-CoV-2 mutation rate and evolution. Possible therapeutics and vaccines against SARS-CoV-2 were proposed. © Copyright 2021 by the Infectious Diseases and Clinical Microbiology Specialty Society of Turkey Mediterranean Journal of Infection, Microbes and Antimicrobials published by Galenos Yayinevi.


ABSTRACT: The outbreak of coronavirus disease 2019 (COVID-19), by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has quickly developed into a worldwide pandemic. Mutations in the SARS-CoV-2 genome may affect various aspects of the disease including fatality ratio. In this study, 553,518 SARS-CoV-2 genome sequences isolated from patients from continents for the period 1 December 2020 to 15 March 2021 were comprehensively analyzed and a total of 82 mutations were identified concerning the reference sequence. In addition, associations between the mutations and the case fatality ratio (CFR), cases per million and deaths per million, were examined. The mutations having the highest frequencies among different continents were Spike_D614G and NSP12_P323L. Among the identified mutations, NSP2_T153M, NSP14_I42V and Spike_L18F mutations showed a positive correlation to CFR. While the NSP13_Y541C, NSP3_T73I and NSP3_Q180H mutations demonstrated a negative correlation to CFR. The Spike_D614G and NSP12_P323L mutations showed a positive correlation to deaths per million. The NSP3_T1198K, NS8_L84S and NSP12_A97V mutations showed a significant negative correlation to deaths per million. The NSP12_P323L and Spike_D614G mutations showed a positive correlation to the number of cases per million. In contrast, NS8_L84S and NSP12_A97V mutations showed a negative correlation to the number of cases per million. In addition, among the identified clades, none showed a significant correlation to CFR. The G, GR, GV, S clades showed a significant positive correlation to deaths per million. The GR and S clades showed a positive correlation to number of cases per million. The clades having the highest frequencies among continents
were G, followed by GH and GR. These findings should be taken into consideration during epidemiological surveys of the virus and vaccine development.

URL: https://www.ncbi.nlm.nih.gov/pubmed/34356077
DOI: 10.3390/genes12071061


ABSTRACT: Wide-scale SARS-CoV-2 genome sequencing is critical to tracking viral evolution during the ongoing pandemic. We develop the software tool, Variant Database (VDB), for quickly examining the changing landscape of spike mutations. Using VDB, we detect an emerging lineage of SARS-CoV-2 in the New York region that shares mutations with previously reported variants. The most common sets of spike mutations in this lineage (now designated as B.1.526) are L5F, T95I, D253G, E484K or S477N, D614G, and A701V. This lineage was first sequenced in late November 2020. Phylodynamic inference confirmed the rapid growth of the B.1.526 lineage. In concert with other variants, like B.1.1.7, the rise of B.1.526 appears to have extended the duration of the second wave of COVID-19 cases in NYC in early 2021. Pseudovirus neutralization experiments demonstrated that B.1.526 spike mutations adversely affect the neutralization titer of convalescent and vaccinee plasma, supporting the public health relevance of this lineage.

URL: https://www.ncbi.nlm.nih.gov/pubmed/34373458
DOI: 10.1038/s41467-021-25168-4


URL: https://www.ncbi.nlm.nih.gov/pubmed/34329674
DOI: 10.1016/j.jinf.2021.07.025


ABSTRACT: Multiple new variants of SARS-CoV-2 have been identified as the COVID-19 pandemic spreads across the globe. However, most epidemic models view the virus as static and unchanging and thus fail to address the consequences of the potential evolution of the virus. Here, we built a competitive susceptible-infected-removed (coSIR) model to simulate the competition between virus strains of differing severities or transmissibility under various virus control policies. The coSIR model predicts that although the virus is extremely unlikely to evolve into a "super virus" that causes an increased fatality rate, virus variants with less severe symptoms can lead to potential new outbreaks and can cost more lives over time. The present model also demonstrates that the protocols restricting the transmission of the virus, such as wearing masks and social distancing, are the most effective strategy in reducing total mortality. A combination of adequate testing and strict quarantine is a powerful alternative to policies such as mandatory stay-at-home orders, which may have an enormous negative impact on the economy. In addition, building Mobile Cabin Hospitals can be effective and efficient in reducing the mortality rate of highly infectious virus strains. Supplementary Information: The online version contains supplementary material available at 10.1007/s11071-021-06705-8.

URL: https://www.ncbi.nlm.nih.gov/pubmed/34334951
DOI: 10.1007/s11071-021-06705-8

ABSTRACT: For epidemic prevention and control, the identification of SARS-CoV-2 subpopulations sharing similar micro-epidemiological patterns and evolutionary histories is necessary for a more targeted investigation into the links among COVID-19 outbreaks caused by SARS-CoV-2 with similar genetic backgrounds. Genomic sequencing analysis has demonstrated the ability to uncover viral genetic diversity. However, an objective analysis is necessary for the identification of SARS-CoV-2 subpopulations. Herein, we detected all the mutations in 186,682 SARS-CoV-2 isolates. We found that the GC content of the SARS-CoV-2 genome had evolved to be lower, which may be conducive to viral spread, and the frameshift mutation was rare in the global population. Next, we encoded the genomic mutations in binary form and used an unsupervised learning classifier, namely PhenoGraph, to classify this information. Consequently, PhenoGraph successfully identified 303 SARS-CoV-2 subpopulations, and we found that the PhenoGraph classification was consistent with, but more detailed and precise than the known GISAID clades (S, L, V, G, GR, GV and O). By the change trend analysis, we found that the growth rate of SARS-CoV-2 diversity has slowed down significantly. We also analyzed the temporal, spatial and phylogenetic relationships among the subpopulations and revealed the evolutionary trajectory of SARS-CoV-2 to a certain extent. Hence, our results provide a better understanding of the patterns and trends in the genomic evolution and epidemiology of SARS-CoV-2.

URL: https://www.ncbi.nlm.nih.gov/pubmed/34382087
DOI: 10.1093/bib/bbab307


ABSTRACT: The present work provides arguments for the involvement of anti-vector immunity and of SARS-CoV-2 variants on the efficacy of ChAdOx1 nCoV-19 vaccine. First, it is suggested that anti-vector immunity takes place as homologous vaccination with ChAdOx1 nCoV-19 vaccine is applied and interferes with vaccine efficacy when the interval between prime and booster doses is less than 3 months. Second, longitudinal studies suggest that ChAdOx1 nCoV-19 vaccine provides suboptimal efficacy against SARS-CoV-2 Alpha variant, which appears to have an increased transmissibility among vaccinated people. At the moment, ChAdOx1 nCoV-19 vaccine is able to reduce the severity of symptoms and transmissibility. However, if the vaccinated individuals do not maintain physical preventive measures, they could turn into potential spreaders, thus suggesting that mass vaccination will not quickly solve the pandemic. Possible consequences of SARS-CoV-2 evolution and of repeated anti-SARS-CoV-2 vaccinations are discussed and adoption of an influenza-like vaccination strategy is suggested.

URL: https://www.ncbi.nlm.nih.gov/pubmed/34331459
DOI: 10.1111/bph.15620


ABSTRACT: SARS-CoV-2 variants of concern (VOCs) have emerged as a global threat to the COVID-19 pandemic response. We implemented a combined approach to quickly detect known VOCs while continuously monitoring for evolving mutations of the virus. To rapidly detect VOCs, two real-time reverse transcriptase PCR assays were designed and implemented, targeting the spike gene H69/V70 deletion and the N501Y mutation. The H69/V70 deletion and N501Y mutation assays demonstrated accuracies of 98.3% (95% CI 93.8 to 99.8) and 100% (95% CI 96.8 to 100), limits of detection of 1,089 and
294 copies/ml, and percent coefficients of variation of 0.08 to 1.16% and 0 to 2.72% for the two gene targets, respectively. No cross-reactivity with common respiratory pathogens was observed with either assay. Implementation of these tests allowed the swift escalation in testing for VOCs from 2.2% to approximately 100% of all SARS-CoV-2-positive samples over 12 January to 9 February 2021, and resulted in the detection of a rapid rise of B.1.1.7 cases within the province of Alberta, Canada. A prospective comparison of the VOC assays to genome sequencing for the detection of B.1.1.7, combined detection of P.1 and B.1.351, and wild-type (i.e., non-VOC) lineages showed sensitivities of 98.2 to 100%, specificities of 98.9 to 100%, positive predictive values of 76.9% to 100%, and negative predictive values of 96 to 100%. Variant screening results inform sampling strategies for regular surveillance by genome sequencing, thus allowing rapid identification of known VOCs while continuously monitoring the evolution of SARS-CoV-2 in the province. IMPORTANCE Different strains, or variants, of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2, the virus that causes COVID-19) have emerged that have higher levels of transmission, less susceptibility to our immune response, and possibly cause more severe disease than previous strains of the virus. Rapid detection of these variants of concern is important to help contain them and prevent them from spreading widely within the population. This study describes two newly developed tests that are able to identify and differentiate the variants of concern from regular strains of SARS-CoV-2. These tests are faster and simpler than the main, gold standard method of identifying variants of concern (genome sequencing). These tests also demonstrated a high correlation with genome sequencing and allowed for the rapid and accurate detection of the rise of B.1.1.7 (one of the variants of concern) in the province of Alberta, Canada.

URL: https://www.ncbi.nlm.nih.gov/pubmed/34378966
DOI: 10.1128/Spectrum.00315-21


URL: https://www.ncbi.nlm.nih.gov/pubmed/34315848
DOI: 10.1038/s41392-021-00695-0
Appendix 1: Evidence Search Details

Filters, Limits & Exclusions: English only  
July 31, 2021 – August 13, 2021

Sources Searched:
- Agency for Clinical Innovation and New South Wales Government
- CanCOVID
- CBC
- CDC
- Center for Infectious Disease Research and Policy (CIDRAP)
- COVID-19 Best Evidence Front Door, University of Michigan
- COVID-19 Immunity Task Force
- COVID-END
- Embase
- European Centres for Disease Prevention and Control (ECDC)
- Google
- Library and Knowledge Services (NHS, England)
- McMaster Plus
- Medline
- National Collaborating Centre for Methods and Tools
- National Health Library & Knowledge Service (Ireland)
- Newfoundland and Labrador Centre for Applied Health Research
- Ontario Science Table
- Prevent Epidemics
- Public Health England
- Public Health Ontario
- Strategy for Patient-Orient Research (SPOR) Evidence Alliance
- UK Government
- Usher Network for COVID-19 Evidence Reviews (UNCOVER), Usher Institute, University of Edinburgh
- Veterans Affairs Evidence Synthesis Program

Librarian(s): Lukas Miller, Clinical Librarian, Saskatchewan Health Authority
Brianna Howell-Spooner, Clinical Librarian, Saskatchewan Health Authority

Appendix 2: Search Strategies

Database: Ovid MEDLINE(R) ALL <1946 to August 12, 2021>
Search Strategy:
--------------------------------------------------------------------------------
1  (coronavirus/ or betacoronavirus/ or coronavirus infections/) and (disease outbreaks/ or epidemics/ or pandemics/) (40069)
2  (nCoV* or 2019nCoV or 19nCoV or COVID19* or COVID or SARS-COV-2 or SARSCOV-2 or SARS-CoV2 or Severe Acute Respiratory Syndrome Coronavirus 2 or Severe Acute Respiratory Syndrome Coronavirus 2).ti,ab,kf,nn,ox,rx,px. (158791)
3  ((new or novel or "19" or "2019" or Wuhan or Hubei or China or Chinese) adj3 (coronavirus* or corona virus* or betacoronavirus* or CoV or HCoV)).ti,ab,kf. (49262)
4  ((coronavirus* or corona virus* or betacoronavirus*) adj3 (pandemic* or epidemic* or outbreak* or crisis)).ti,ab,kf. (9109)
5  ((Wuhan or Hubei) adj5 pneumonia).ti,ab,kf. (355)
6  or/1-5 (165005)
Evidence Search Report: EOC031801v11 ESR

Database: Embase <1974 to 2021 August 12>
Search Strategy:

1. (exp coronaviridae infection/ or exp coronavirinae/ or exp coronavirus disease 2019/ or exp coronavirus infection/) and (epidemic/ or pandemic/) (70400)
2. (nCoV* or 2019nCoV or 19nCoV or COVID19* or COVID or SARS-COV-2 or SARS-CoV2 or Severe Acute Respiratory Syndrome Coronavirus 2 or Severe Acute Respiratory Syndrome Coronavirus 2).mp. (161174)
3. ((new or novel or "19" or "2019" or Wuhan or Hubei or China or Chinese) adj3 (coronavirus* or corona virus* or betacoronavirus* or CoV or HCoV)).ti,ab,kw. (47665)
4. ((coronavirus* or corona virus* or betacoronavirus*) adj3 (pandemic* or epidemic* or outbreak* or crisis))).ti,ab,kw. (47665)
5. ((Wuhan or Hubei) adj5 pneumonia).ti,ab,kw. (395)
Evidence Search Report: EOC031801v11 ESR

6 or/1-5 (172257)
7 6 and (WHO adj2 (alpha or beta or gamma or delta or lambda)).ti.kw. [WHO VOC] (1)
8 ((british or UK or united kingdom or england or english or south african or south africa or brazil or Brazilian or brasil or brasilian or california? or new york or india?) adj2 (strain? or mutation? or variant?!)).ti.kw. (954)
9 ((variant? or mutation? or strain? or lineage?) adj2 (virus* or viral* or coronavirus* or COVID-19 or SARS-COV-2 or COVID19 or nCoV* or "of concern" or "of interest").ti.kw. (7097)
10 (genetic or new or newer or newest or novel) adj1 (variant or mutation? or lineage? or strain?!).ti.kw. (18947)
11 ("20I/S:501Y.V1" or "20I/501Y.V1" or "B.1.1.7" or "B117" or "501YV1" or "GR/501Y.V1" or "GRY" or (alpha adj1 variant?!)).ti.kw. [WHO Alpha] (305)
12 ("B.1.351" or "B1351" or "20H/501Y.V2" or "GH/501Y.V2" or "20H/501Y.V2" or "501YV2" or (beta adj1 variant?!)).ti.kw. [WHO Beta] (153)
13 ("P.1" or "P1" or "20I/501Y.V3" or "501YV3" or "GR/501Y.V3" or "20J/501Y.V3" or (gamma adj1 variant?!)).ti.kw. [WHO Gamma] (5089)
14 ("B.1.617.2" or "B16172" or "G/452R.V3" or "G/452RV3" or "G452RV3" or "G452R.V3" or "21A/S:478K" or (delta adj1 variant?!)).ti.kw. [WHO Delta] (43)
15 ((lambda adj1 variant?!) or "GR/452Q.V1").ti.kw. (5)
16 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 [All WHO Variants of Concern] (32157)
17 (WHO adj2 (epsilon or zeta or eta or theta or iota or kappa)).ti.kw. [WHO VOI] (0)
18 ("B.1.427" or "B.1.429" or "B.1.427/B.1.429" or "GH/452R.V1" or "20C/S.484R" or (epsilon adj1 variant?!)).ti.kw. [WHO Epsilon] (18)
19 ("P.2" or "P2" or "GR" or "20B/S.484K" or (zeta adj1 variant?!)).ti.kw. [WHO Zeta] (7153)
20 ("B.1.525" or "B1525" or "G/452K.V3" or "20A/S484K" or (eta adj1 variant?!)).ti.kw. [WHO Eta] (2)
21 ("P.3" or "P3" or "GR" or "20B/S:265C" or (theta adj1 variant?!)).ti.kw. [WHO Theta] (5411)
22 ("B.1.526" or "B1526" or "GH" or "20C/S.484R" or (iota adj1 variant?!)).ti.kw. [WHO Iota] (10025)
23 ("B.1.617.1" or "B16171" or "G/452R.V3" or "21A/S:154K" or (kappa adj1 variant?!)).ti.kw. (5)
24 (or/17-23) and (variant? or lineage? or clade? or mutation?!).ti.kw. [All WHO Variants of Interest] (509)
25 16 or 24 [All VOC/VOI] (32622)
26 6 and 25 (1078)
27 limit 26 to dd=20210730-20210813 (107)
28 limit 27 to medline (40)
29 27 not 28 (67)
30 limit 29 to english language (66)
31 from 30 keep 1-66 (66)

Other Sources
COVID AND [variant* OR delta OR alpha OR beta OR lambda]