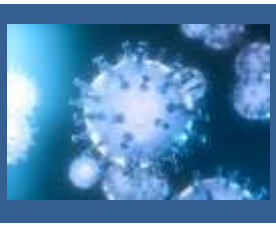
COVID-19

Oct 21 – 27, 2021



RESEARCH PUBLICATIONS

Publication Date: Oct 27, 2021

The impact of school opening model on SARS-CoV-2 community incidence and mortality

Abstract

The role that traditional and hybrid in-person schooling modes contribute to the community incidence of SARS-CoV-2 infections relative to fully remote schooling is unknown. We conducted an event study using a retrospective nationwide cohort evaluating the effect of school mode on SARS-CoV-2 cases during the 12 weeks after school opening (July–September 2020, before the Delta variant was predominant), stratified by US Census region. After controlling for case rate trends before school start, state-level mitigation measures and community activity level, SARS-CoV-2 incidence rates were not statistically different in counties with in-person learning versus remote school modes in most regions of the United States. In the South, there was a significant and sustained increase in cases per week among counties that opened in a hybrid or traditional mode versus remote, with weekly effects ranging from 9.8 (95% confidence interval (CI) = 2.7–16.1) to 21.3 (95% CI = 9.9–32.7) additional cases per 100,000 persons, driven by increasing cases among 0–9 year olds and adults. Schools can reopen for in-person learning without substantially increasing community case rates of SARS-CoV-2; however, the impacts are variable. Additional studies are needed to elucidate the underlying reasons for the observed regional differences more fully.

Reference

https://www.nature.com/articles/s41591-021-01563-8

Functional antibody and T cell immunity following SARS-CoV-2 infection, including by variants of concern, in patients with cancer: The CAPTURE study

Abstract

Patients with cancer have higher COVID-19 morbidity and mortality. Here we present the prospective CAPTURE study, integrating longitudinal immune profiling with clinical annotation. Of 357 patients with cancer, 118 were SARS-CoV-2 positive, 94 were symptomatic and 2 died of COVID-19. In this cohort, 83% patients had S1-reactive antibodies and 82% had neutralizing antibodies against wild type SARS-CoV-2, whereas neutralizing antibody titers against the Alpha, Beta and Delta variants were substantially reduced. S1-reactive antibody levels decreased in 13% of patients, whereas neutralizing antibody titers remained stable for up to 329 days. Patients also had detectable SARS-CoV-2-specific T cells and CD4+ responses correlating with S1-reactive antibody levels, although patients with hematological malignancies had impaired immune responses that were disease and treatment specific, but presented compensatory cellular responses, further supported by clinical recovery in all but one patient. Overall, these findings advance the understanding of the nature and duration of the immune response to SARS-CoV-2 in patients with cancer.

Reference

https://www.nature.com/articles/s43018-021-00275-9

Adaptive immunity and neutralizing antibodies against SARS-CoV-2 variants of concern following vaccination in patients with cancer: The CAPTURE study

Abstract

Coronavirus disease 2019 (COVID-19) antiviral response in a pan-tumor immune monitoring (CAPTURE) (NCT03226886) is a prospective cohort study of COVID-19 immunity in patients with cancer. Here we evaluated 585 patients following administration of two doses of BNT162b2 or AZD1222 vaccines, administered 12 weeks apart. Seroconversion rates after two doses were 85% and 59% in patients with solid and hematological malignancies, respectively. A lower proportion of patients had detectable titers of neutralizing antibodies (NAbT) against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants of concern (VOC) versus wild-type

(WT) SARS-CoV-2. Patients with hematological malignancies were more likely to have undetectable NAbT and had lower median NAbT than those with solid cancers against both SARS-CoV-2 WT and VOC. By comparison with individuals without cancer, patients with hematological, but not solid, malignancies had reduced neutralizing antibody (NAb) responses. Seroconversion showed poor concordance with NAbT against VOC. Previous SARS-CoV-2 infection boosted the NAb response including against VOC, and anti-CD20 treatment was associated with undetectable NAbT. Vaccine-induced T cell responses were detected in 80% of patients and were comparable between vaccines or cancer types. Our results have implications for the management of patients with cancer during the ongoing COVID-19 pandemic.

Reference

https://www.nature.com/articles/s43018-021-00274-w

A machine-learning parsimonious multivariable predictive model of mortality risk in patients with COVID-19

Abstract

The COVID-19 pandemic is impressively challenging the healthcare system. Several prognostic models have been validated but few of them are implemented in daily practice. The objective of the study was to validate a machine-learning risk prediction model using easy-to-obtain parameters to help to identify patients with COVID-19 who are at higher risk of death. The training cohort included all patients admitted to Fondazione Policlinico Gemelli with COVID-19 from March 5, 2020, to November 5, 2020. Afterward, the model was tested on all patients admitted to the same hospital with COVID-19 from November 6, 2020, to February 5, 2021. The primary outcome was in-hospital case-fatality risk. The out-of-sample performance of the model was estimated from the training set in terms of Area under the Receiving Operator Curve (AUROC) and classification matrix statistics by averaging the results of fivefold cross validation repeated 3-times and comparing the results with those obtained on the test set. An explanation analysis of the model, based on the SHapley Additive exPlanations (SHAP), is also presented. To assess the subsequent time evolution, the change in paO2/FiO2 (P/F) at 48 h after the baseline measurement was plotted against its baseline value. Among the 921 patients included in the training cohort, 120 died (13%). Variables

selected for the model were age, platelet count, SpO2, blood urea nitrogen (BUN), hemoglobin, C-reactive protein, neutrophil count, and sodium. The results of the fivefold cross-validation repeated 3-times gave AUROC of 0.87, and statistics of the classification matrix to the Youden index as follows: sensitivity 0.840, specificity 0.774, negative predictive value 0.971. Then, the model was tested on a new population (n = 1463) in which the case-fatality rate was 22.6%. The test model showed AUROC 0.818, sensitivity 0.813, specificity 0.650, negative predictive value 0.922. Considering the first quartile of the predicted risk score (low-risk score group), the case-fatality rate was 1.6%, 17.8% in the second and third quartile (high-risk score group) and 53.5% in the fourth quartile (very high-risk score group). The three risk score groups showed good discrimination for the P/F value at admission, and a positive correlation was found for the low-risk class to P/F at 48 h after admission (adjusted R-squared = 0.48). We developed a predictive model of death for people with SARS-CoV-2 infection by including only easy-to-obtain variables (abnormal blood count, BUN, C-reactive protein, sodium and lower SpO2). It demonstrated good accuracy and high power of discrimination. The simplicity of the model makes the risk prediction applicable for patients in the Emergency Department, or during hospitalization. Although it is reasonable to assume that the model is also applicable in not-hospitalized persons, only appropriate studies can assess the accuracy of the model also for persons at home.

Reference

https://www.nature.com/articles/s41598-021-99905-6

IFNL4 genetic variant can predispose to COVID-19

Abstract

Interferon lambda 4 (IFNλ4) has shown antiviral activity against RNA viruses, including some coronaviruses. Besides, genetic variants of IFNL4 can be predictive of the clearance of RNA viruses. However, little is known about the effect of these genetic variants on SARS-CoV-2 infection. In this study, we investigated whether there was a relationship of the rs12979860 polymorphism of IFNL4 with COVID-19. We found that the T allele of rs12979860 was overexpressed in COVID-19 patients with regard to the general population without this disease (36.16% vs. 26.40%, p = 6.4 × 10–4; OR 0.633 C vs T; 95% CI 0.487, 0.824), suggesting that this allele could be a risk factor for COVID-

19. Accordingly, the CC genotype was significantly lower in COVID-19 patients compared to controls (37.85% vs. 55.51%, $p = 8 \times 10–5$; OR 0.488; 95% CI 0.342, 0.698). These results were not affected by sex, age, and disease severity in patients with COVID-19. Our findings suggest that, like other infectious diseases caused by RNA viruses, genetic variants of IFNL4 can predispose to COVID-19. Confirmation of our results may contribute to better understanding the mechanisms of this disease.

Reference

https://www.nature.com/articles/s41598-021-00747-z

Household transmission of COVID-19 cases associated with SARS-CoV-2 delta variant (B.1.617.2): National case-control study

Abstract

Background: The SARS-CoV-2 Delta variant (B.1.617.2), first detected in India, has rapidly become the dominant variant in England. Early reports suggest this variant has an increased growth rate suggesting increased transmissibility. This study indirectly assessed differences in transmissibility between the emergent Delta variant compared to the previously dominant Alpha variant (B.1.1.7).

Methods: A matched case-control study was conducted to estimate the odds of household transmission (≥ 2 cases within 14 days) for Delta variant index cases compared with Alpha cases. Cases were derived from national surveillance data (March to June 2021). One-to-two matching was undertaken on geographical location of residence, time period of testing and property type, and a multivariable conditional logistic regression model was used for analysis.

Findings: In total 5,976 genomically sequenced index cases in household clusters were matched to 11,952 sporadic index cases (single case within a household). 43.3% (n=2,586) of cases in household clusters were confirmed Delta variant compared to 40.4% (n= 4,824) of sporadic cases. The odds ratio of household transmission was 1.70 among Delta variant cases (95% CI 1.48-1.95, p <0.001) compared to Alpha cases after adjusting for age, sex, ethnicity, index of multiple deprivation (IMD), number of household contacts and vaccination status of index case.

Interpretation: We found evidence of increased household transmission of SARS-CoV-2 Delta variant, potentially explaining its success at displacing Alpha variant as the dominant strain in England. With the Delta variant now having been detected in many countries worldwide, the understanding of the transmissibility of this variant is important for informing infection prevention and control policies internationally.

Reference

https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762(21)00238-6/fulltext

Publication Date: Oct 26, 2021

Data-driven analysis of amino acid change dynamics timely reveals SARS-CoV-2 variant emergence

Abstract

Since its emergence in late 2019, the diffusion of SARS-CoV-2 is associated with the evolution of its viral genome. The co-occurrence of specific amino acid changes, collectively named ‘virus variant’, requires scrutiny (as variants may hugely impact the agent’s transmission, pathogenesis, or antigenicity); variant evolution is studied using phylogenetics. Yet, never has this problem been tackled by digging into data with ad hoc analysis techniques. Here we show that the emergence of variants can in fact be traced through data-driven methods, further capitalizing on the value of large collections of SARS-CoV-2 sequences. For all countries with sufficient data, we compute weekly counts of amino acid changes, unveil time-varying clusters of changes with similar—rapidly growing—dynamics, and then follow their evolution. Our method succeeds in timely associating clusters to variants of interest/concern, provided their change composition is well characterized. This allows us to detect variants’ emergence, rise, peak, and eventual decline under competitive pressure of another variant. Our early warning system, exclusively relying on deposited sequences, shows the power of big data in this context, and concurs to calling for the wide spreading of public SARS-CoV-2 genome sequencing for improved surveillance and control of the COVID-19 pandemic.

Reference

https://www.nature.com/articles/s41598-021-00496-z

SARS-CoV-2 exploits host DGAT and ADRP for efficient replication

Abstract

Coronavirus Disease 2019 (COVID-19) is predominantly a respiratory tract infection that significantly rewires the host metabolism. Here, we monitored a cohort of COVID-19 patients' plasma lipidome over the disease course and identified triacylglycerol (TG) as the dominant lipid class present in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-induced metabolic dysregulation. In particular, we pinpointed the lipid droplet (LD)-formation enzyme diacylglycerol acyltransferase (DGAT) and the LD stabilizer adipocyte differentiation-related protein (ADRP) to be essential host factors for SARS-CoV-2 replication. Mechanistically, viral nucleo capsid protein drives DGAT1/2 gene expression to facilitate LD formation and associates with ADRP on the LD surface to complete the viral replication cycle. DGAT gene depletion reduces SARS-CoV-2 protein synthesis without compromising viral genome replication/transcription. Importantly, a cheap and orally available DGAT inhibitor, xanthohumol, was found to suppress SARS-CoV-2 replication and the associated pulmonary inflammation in a hamster model. Our findings not only uncovered the mechanistic role of SARS-CoV-2 nucleocapsid protein to exploit LDs-oriented network for heightened metabolic demand, but also the potential to target the LDs-synthetase DGAT and LDs-stabilizer ADRP for COVID-19 treatment.

Reference

https://www.nature.com/articles/s41421-021-00338-2

Host methylation predicts SARS-CoV-2 infection and clinical outcome

Abstract

Background: Since the onset of the SARS-CoV-2 pandemic, most clinical testing has focused on RT-PCR1. Host epigenome manipulation post coronavirus infection2,3,4 suggests that DNA methylation signatures may differentiate patients with SARS-CoV-2 infection from uninfected individuals, and help predict COVID-19 disease severity, even at initial presentation.

Methods: We customized Illumina's Infinium MethylationEPIC array to enhance immune response detection and profiled peripheral blood samples from 164 COVID-19 patients with longitudinal measurements of disease severity and 296 patient controls.

Results: Epigenome-wide association analysis revealed 13,033 genome-wide significant methylation sites for case-vs-control status. Genes and pathways involved in interferon signaling and viral response were significantly enriched among differentially methylated sites. We observe highly significant associations at genes previously reported in genetic association studies (e.g. IRF7, OAS1). Using machine learning techniques, models built using sparse regression yielded highly predictive findings: cross-validated best fit AUC was 93.6% for case-vs-control status, and 79.1%, 80.8%, and 84.4% for hospitalization, ICU admission, and progression to death, respectively.

Conclusions: In summary, the strong COVID-19-specific epigenetic signature in peripheral blood driven by key immune-related pathways related to infection status, disease severity, and clinical deterioration provides insights useful for diagnosis and prognosis of patients with viral infections.

Reference

https://www.nature.com/articles/s43856-021-00042-y

Comprehensive investigations revealed consistent pathophysiological alterations after vaccination with COVID-19 vaccines

Abstract

Large-scale COVID-19 vaccinations are currently underway in many countries in response to the COVID-19 pandemic. Here, we report, besides generation of neutralizing antibodies, consistent alterations in hemoglobin A1c, serum sodium and potassium levels, coagulation profiles, and renal functions in healthy volunteers after vaccination with an inactivated SARS-CoV-2 vaccine. Similar changes had also been reported in COVID-19 patients, suggesting that vaccination mimicked an infection. Single-cell mRNA sequencing (scRNA-seq) of peripheral blood mononuclear cells (PBMCs) before and 28 days after the first inoculation also revealed consistent alterations in gene expression of many different immune cell types. Reduction of CD8+ T cells and increase in classic monocyte contents were exemplary. Moreover, scRNA-

seq revealed increased NF-κB signaling and reduced type I interferon responses, which were confirmed by biological assays and also had been reported to occur after SARS-CoV-2 infection with aggravating symptoms. Altogether, our study recommends additional caution when vaccinating people with pre-existing clinical conditions, including diabetes, electrolyte imbalances, renal dysfunction, and coagulation disorders.

Reference

https://www.nature.com/articles/s41421-021-00329-3

Membrane fusion and immune evasion by the spike protein of SARS-CoV-2 Delta variant

Abstract

The Delta variant of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has outcompeted previously prevalent variants and become a dominant strain worldwide. We report the structure, function, and antigenicity of its full-length spike (S) trimer and those of the Gamma and Kappa variants and compare their characteristics with the G614, Alpha, and Beta variants. Delta S can fuse membranes more efficiently at low levels of cellular receptor ACE2, and its pseudotyped viruses infect target cells substantially faster than the other five variants, possibly accounting for its heightened transmissibility. Each variant shows different rearrangement of the antigenic surface of the N-terminal domain of the S protein, but only causes local changes in the receptor-binding domain (RBD), making the RBD a better target for therapeutic antibodies.

Abstract

https://www.science.org/doi/10.1126/science.abl9463

Immune memory from SARS-CoV-2 infection in hamsters provides variant-independent protection but still allows virus transmission

Abstract

SARS-CoV-2 has caused significant morbidity and mortality across the globe. As the virus spreads, new variants are arising that show enhanced capacity to bypass pre-existing immunity. To understand the memory response to SARS-CoV-2, here we monitored SARS-CoV-2-specific T and B cells in a longitudinal study of infected and

recovered golden hamsters. We demonstrated that engagement of the innate immune system following SARS-CoV-2 infection was delayed but was followed by a pronounced adaptive response. Moreover, T cell adoptive transfer conferred a reduction in virus levels and rapid induction of SARS-CoV-2-specific B cells demonstrating both lymphocyte populations contributed to the overall response. Re-infection of recovered animals with a SARS-CoV-2 variant of concern showed that SARS-CoV-2-specific T and B cells could effectively control the infection which associated with the rapid induction of neutralizing antibodies but failed to block transmission to both naïve and seroconverted animals. These data suggest that the adaptive immune response to SARS-CoV-2 is sufficient to provide protection to the host, independent of the emergence of novel variants.

Reference

https://www.science.org/doi/10.1126/sciimmunol.abm3131

Publication Date: Oct 25, 2021

Intranasal delivery of replicating mRNA encoding neutralizing antibody against SARS-CoV-2 infection in mice

Abstract

The lung is the prophylaxis target against SARS-CoV-2 infection, and neutralizing antibodies are a leading class of biological products against various infectious viral pathogen. In this study, we develop a safe and cost-effective platform to express neutralizing antibody in the lung with replicating mRNA basing on alphavirus replicon particle (VRP) delivery system, to prevent SARS-CoV-2 infections. First, a modified VEEV replicon with two subgenomic (sg) promoters was engineered to translate the light and heavy chains of antibody simultaneously, for expression and assembly of neutralizing anti-SARS-CoV-2 antibody CB6. Second, the feasibility and protective efficacy of replicating mRNA against SARS-CoV-2 infection were demonstrated through both in vitro and in vivo assays. The lung target delivery with the help of VRP system resulted in efficiently block SARS-CoV-2 infection with reducing viral titer and less tissue damage in the lung of mice. Overall, our data suggests that expressing neutralizing

antibodies in the lungs with the help of self-replicating mRNA could potentially be a promising prophylaxis approach against SARS-CoV-2 infection.

Reference

https://www.nature.com/articles/s41392-021-00783-1

Neurological complications after first dose of COVID-19 vaccines and SARS-CoV-2 infection

Abstract

Emerging reports of rare neurological complications associated with COVID-19 infection and vaccinations are leading to regulatory, clinical and public health concerns. We undertook a self-controlled case series study to investigate hospital admissions from neurological complications in the 28 days after a first dose of ChAdOx1nCoV-19 (n = 20,417,752) or BNT162b2 (n = 12,134,782), and after a SARS-CoV-2-positive test (n = 2,005,280). There was an increased risk of Guillain–Barré syndrome (incidence rate ratio (IRR), 2.90; 95% confidence interval (CI): 2.15–3.92 at 15–21 days after vaccination) and Bell's palsy (IRR, 1.29; 95% CI: 1.08–1.56 at 15–21 days) with ChAdOx1nCoV-19. There was an increased risk of hemorrhagic stroke (IRR, 1.38; 95% CI: 1.12–1.71 at 15–21 days) with BNT162b2. An independent Scottish cohort provided further support for the association between ChAdOx1nCoV and Guillain–Barré syndrome (IRR, 2.32; 95% CI: 1.08–5.02 at 1–28 days). There was a substantially higher risk of all neurological outcomes in the 28 days after a positive SARS-CoV-2 test including Guillain–Barré syndrome (IRR, 5.25; 95% CI: 3.00–9.18). Overall, we estimated 38 excess cases of Guillain–Barré syndrome per 10 million people receiving ChAdOx1nCoV-19 and 145 excess cases per 10 million people after a positive SARS-CoV-2 test. In summary, although we find an increased risk of neurological complications in those who received COVID-19 vaccines, the risk of these complications is greater following a positive SARS-CoV-2 test.

Reference

https://www.nature.com/articles/s41591-021-01556-7

Resistance of SARS-CoV-2 variants to neutralization by convalescent plasma from early COVID-19 outbreak in Singapore

Abstract

The rapid spreading of SARS-CoV-2 variants B.1.1.7 originated from the United Kingdom and B.1.351 from South Africa has contributed to the second wave of COVID-19 cases in the respective countries and also around the world. In this study, we employed advanced biochemical and virological methodologies to evaluate the impact of Spike mutations of these strains on the degree of protection afforded by humoral immune responses following natural infection of the ancestral SARS-CoV-2 strain during the early stages of the outbreak. We found that antibody-mediated neutralization activity was partially reduced for B.1.1.7 variant and significantly attenuated for the B.1.351 strain. We also found that mutations outside the receptor-binding domain (RBD) can strongly influence antibody binding and neutralization, cautioning the use of solely RBD mutations in evaluating vaccine efficacy. These findings highlight an urgent need to develop new SARS-CoV-2 vaccines that are not based exclusively on the ancestral SARS-CoV-2 Spike gene sequence.

Reference

https://www.nature.com/articles/s41541-021-00389-2

Cryptic transmission of SARS-CoV-2 and the first COVID-19 wave

Abstract

Considerable uncertainty surrounds the timeline of introductions and onsets of local transmission of SARS-CoV-2 globally. Although a limited number of SARS-CoV-2 introductions were reported in January and February 2020, the narrowness of the initial testing criteria, combined with a slow growth in testing capacity and porous travel screening, left many countries vulnerable to unmitigated, cryptic transmission. Here we use a global metapopulation epidemic model to provide a mechanistic understanding of the early dispersal of infections, and the temporal windows of the introduction and onset of SARS-CoV-2 local transmission in Europe and the United States. We find that community transmission of SARS-CoV-2 was likely in several areas of Europe and the United States by January 2020, and estimate that by early March, only 1 to 3 in 100

SARS-CoV-2 infections were detected by surveillance systems. The modelling results highlight international travel as the key driver of the introduction of SARS-CoV-2 with possible introductions and transmission events as early as December 2019–January 2020. We find a heterogeneous, geographic distribution of cumulative infection attack rates by 4 July 2020, ranging from 0.78%–15.2% across US states and 0.19%–13.2% in European countries. Our approach complements phylogenetic analyses and other surveillance approaches and provides insights that can be used to design innovative, model-driven surveillance systems that guide enhanced testing and response strategies.

Reference

https://www.nature.com/articles/s41586-021-04130-w

Publication Date: Oct 22, 2021

Accurate detection and quantification of SARS-CoV-2 genomic and subgenomic mRNAs by ddPCR and meta-transcriptomics analysis

Abstract

SARS-CoV-2 replication requires the synthesis of a set of structural proteins expressed through discontinuous transcription of ten subgenomic mRNAs (sgmRNAs). Here, we have fine-tuned droplet digital PCR (ddPCR) assays to accurately detect and quantify SARS-CoV-2 genomic ORF1ab and sgmRNAs for the nucleocapsid (N) and spike (S) proteins. We analyzed 166 RNA samples from anonymized SARS-CoV-2 positive subjects and we observed a recurrent and characteristic pattern of sgmRNAs expression in relation to the total viral RNA content. Additionally, expression profiles of sgmRNAs, as determined by meta-transcriptomics sequencing of a subset of 110 RNA samples, were highly correlated with those obtained by ddPCR. By providing a comprehensive and dynamic snapshot of the levels of SARS-CoV-2 sgmRNAs in infected individuals, our results may contribute a better understanding of the dynamics of transcription and expression of the genome of SARS-CoV-2 and facilitate the development of more accurate molecular diagnostic tools for the stratification of COVID-19 patients.

Reference

https://www.nature.com/articles/s42003-021-02748-0

Genomic epidemiology and the role of international and regional travel in the SARS-CoV-2 epidemic in Zimbabwe: A retrospective study of routinely collected surveillance data

Abstract

Background: Advances in SARS-CoV-2 sequencing have enabled identification of new variants, tracking of its evolution, and monitoring of its spread. We aimed to use whole genome sequencing to describe the molecular epidemiology of the SARS-CoV-2 outbreak and to inform the implementation of effective public health interventions for control in Zimbabwe.

Methods: We performed a retrospective study of nasopharyngeal samples collected from nine laboratories in Zimbabwe between March 20 and Oct 16, 2020. Samples were taken as a result of quarantine procedures for international arrivals or to test for infection in people who were symptomatic or close contacts of positive cases. Samples that had a cycle threshold of less than 30 in the diagnostic PCR test were processed for sequencing. We began our analysis in July, 2020 (120 days since the first case), with a follow-up in October, 2020 (at 210 days since the first case). The phylogenetic relationship of the genome sequences within Zimbabwe and global samples was established using maximum likelihood and Bayesian methods.

Findings: Of 92 299 nasopharyngeal samples collected during the study period, 8099 were PCR-positive and 328 were available for sequencing, with 156 passing sequence quality control. 83 (53%) of 156 were from female participants. At least 26 independent introductions of SARS-CoV-2 into Zimbabwe in the first 210 days were associated with 12 global lineages. 151 (97%) of 156 had the Asp614Gly mutation in the spike protein. Most cases, 93 (60%), were imported from outside Zimbabwe. Community transmission was reported 6 days after the onset of the outbreak.

Interpretation: Initial public health interventions delayed onset of SARS-CoV-2 community transmission after the introduction of the virus from international and

regional migration in Zimbabwe. Global whole genome sequence data are essential to reveal major routes of spread and guide intervention strategies.

Reference

https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(21)00434-4/fulltext

Publication Date: Oct 21, 2021

Immunogenicity and efficacy of heterologous ChadOx1/BNT162b2 vaccination

Abstract

Following severe adverse reactions to the AstraZeneca ChAdOx1-S-nCoV-19 vaccine, European health authorities have recommended that patients under the age of 55 who received one dose of ChAdOx1-S-nCoV-19 vaccine receive a second dose of Pfizer BNT162b2 vaccine as a booster. However, the effectiveness and the immunogenicity of this vaccination regimen have not been formally tested. Here, we show that the heterologous ChAdOx1-S-nCoV-19/BNT162b2 combination confers better protection against Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) infection than the homologous BNT162b2/BNT162b2 combination in a real-world observational study of healthcare workers (n=13121). To understand the underlying mechanism, we conducted a longitudinal survey of the anti-spike immunity conferred by each vaccine combination. Both combinations induced strong anti-spike antibody (Ab) responses but sera from heterologous vaccinated individuals displayed a stronger neutralizing activity, regardless of the SARS-CoV-2 variant. This enhanced neutralizing potential was correlated with increased frequencies of switched and activated memory B cells recognizing the SARS-CoV-2 Receptor Binding Domain (RBD). The ChAdOx1-S-nCoV-19 vaccine induced a weaker IgG response but a stronger T cell response than the BNT162b2 vaccine after the priming dose, which could explain the complementarity of both vaccines when used in combination. The heterologous vaccination regimen could therefore be particularly suitable for immune compromised individuals.

Reference

https://www.nature.com/articles/s41586-021-04120-y

The SARS-CoV-2 main protease M^{pro} causes microvascular brain pathology by cleaving NEMO in brain endothelial cells

Abstract

Coronavirus disease 2019 (COVID-19) can damage cerebral small vessels and cause neurological symptoms. Here we describe structural changes in cerebral small vessels of patients with COVID-19 and elucidate potential mechanisms underlying the vascular pathology. In brains of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-infected individuals and animal models, we found an increased number of empty basement membrane tubes, so-called string vessels representing remnants of lost capillaries. We obtained evidence that brain endothelial cells are infected and that the main protease of SARS-CoV-2 (Mpro) cleaves NEMO, the essential modulator of nuclear factor-κB. By ablating NEMO, Mpro induces the death of human brain endothelial cells and the occurrence of string vessels in mice. Deletion of receptor-interacting protein kinase (RIPK) 3, a mediator of regulated cell death, blocks the vessel rarefaction and disruption of the blood–brain barrier due to NEMO ablation. Importantly, a pharmacological inhibitor of RIPK signaling prevented the Mpro-induced microvascular pathology. Our data suggest RIPK as a potential therapeutic target to treat the neuropathology of COVID-19.

Reference

https://www.nature.com/articles/s41593-021-00926-1

Vitamin D-related polymorphisms and vitamin D levels as risk biomarkers of COVID-19 disease severity

Abstract

Vitamin D is a fundamental regulator of host defences by activating genes related to innate and adaptive immunity. Previous research shows a correlation between the levels of vitamin D in patients infected with SARS-CoV-2 and the degree of disease severity. This work investigates the impact of the genetic background related to vitamin D pathways on COVID-19 severity. For the first time, the Portuguese population was characterized regarding the prevalence of high impact variants in genes associated with the vitamin D pathways. This study enrolled 517 patients admitted to two tertiary

Portuguese hospitals. The serum concentration of 25 (OH)D, was measured in the hospital at the time of patient admission. Genetic variants, 18 variants, in the genes AMDHD1, CYP2R1, CYP24A1, DHCR7, GC, SEC23A, and VDR were analysed. The results show that polymorphisms in the vitamin D binding protein encoded by the GC gene are related to the infection severity ($p = 0.005$). There is an association between vitamin D polygenic risk score and the serum concentration of 25 (OH)D ($p = 0.04$). There is an association between 25 (OH)D levels and the survival and fatal outcomes ($p = 1.5e{-}4$). The Portuguese population has a higher prevalence of the DHCR7 RS12785878 variant when compared with its prevalence in the European population (19% versus 10%). This study shows a genetic susceptibility for vitamin D deficiency that might explain higher severity degrees in COVID-19 patients. These results reinforce the relevance of personalized strategies in the context of viral diseases.

Reference

https://www.nature.com/articles/s41598-021-99952-z

Emerging SARS-CoV-2 variants expand species tropism to murines

Abstract

Background: Wildtype mice are not susceptible to SARS-CoV-2 infection. Emerging SARS-CoV-2 variants, including B.1.1.7, B.1.351, P.1, and P.3, contain mutations in spike that has been suggested to associate with an increased recognition of mouse ACE2, raising the postulation that these SARS-CoV-2 variants may have evolved to expand species tropism to wildtype mouse and potentially other murines. Our study evaluated this possibility with substantial public health importance.

Methods: We investigated the capacity of wildtype (WT) SARS-CoV-2 and SARS-CoV-2 variants in infecting mice (Mus musculus) and rats (Rattus norvegicus) under in vitro and in vivo settings. Susceptibility to infection was evaluated with RT-qPCR, plaque assays, immunohistological stainings, and neutralization assays.

Findings: Our results reveal that B.1.1.7 and other N501Y-carrying variants but not WT SARS-CoV-2 can infect wildtype mice. High viral genome copies and high infectious virus particle titres are recovered from the nasal turbinate and lung of B.1.1.7-inocluated mice for 4-to-7 days post infection. In agreement with these observations, robust

expression of viral nucleocapsid protein and histopathological changes are detected from the nasal turbinate and lung of B.1.1.7-inocluated mice but not that of the WT SARS-CoV-2-inoculated mice. Similarly, B.1.1.7 readily infects wildtype rats with production of infectious virus particles.

Interpretation: Our study provides direct evidence that the SARS-CoV-2 variant, B.1.1.7, as well as other N501Y-carrying variants including B.1.351 and P.3, has gained the capability to expand species tropism to murines and public health measures including stringent murine control should be implemented to facilitate the control of the ongoing pandemic.

Reference

https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(21)00436-9/fulltext