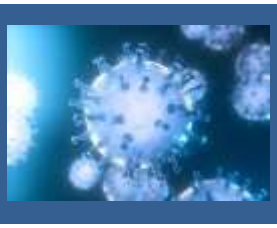
COVID-19

Jul 08 – 14, 2021



RESEARCH PUBLICATIONS

Publication Date: Jul 14, 2021

Immune responses against SARS-CoV-2 variants after heterologous and homologous ChAdOx1 nCoV-19/BNT162b2 vaccination

Abstract

Currently approved viral vector-based and mRNA-based vaccine approaches against coronavirus disease 2019 (COVID-19) consider only homologous prime-boost vaccination. After reports of thromboembolic events, several European governments recommended using AstraZeneca's ChAdOx1-nCov-19 (ChAd) only in individuals older than 60 years, leaving millions of already ChAd-primed individuals with the decision to receive either a second shot of ChAd or a heterologous boost with mRNA-based vaccines. However, such combinations have not been tested so far. Hannover Medical School's COVID-19 Contact Study cohort of healthcare professionals was used to monitor ChAd-primed immune responses before and 3 weeks after booster with ChAd (n = 32) or BioNTech/Pfizer's BNT162b2 (n = 55). Although both vaccines boosted prime-induced immunity, BNT162b2 induced significantly higher frequencies of spike-specific CD4+ and CD8+ T cells and, in particular, high titers of neutralizing antibodies against the B.1.1.7, B.1.351 and P.1 variants of concern of severe acute respiratory syndrome coronavirus 2.

Reference

https://www.nature.com/articles/s41591-021-01449-9

Neutralising SARS-CoV-2 RBD-specific antibodies persist for at least six months independently of symptoms in adults

Abstract

Background: In spring 2020, at the beginning of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic in Europe, we set up an assay system for large-scale testing of virus-specific and neutralising antibodies including their longevity.

Methods: The sera of 1655 adult employees for SARS-CoV-2-specific antibodies were analysed using the S1 subunit of the spike protein of SARS-CoV-2. Sera containing S1-reactive antibodies were further evaluated for receptor-binding domain (RBD)- and nucleocapsid protein (NCP)-specific antibodies in relation to the neutralisation test (NT) results at three time points over six months.

Results: Immunoglobulin G (IgG) and/or IgA antibodies reactive to the S1 protein in 10.15% (n = 168) of the participants, were detected. In total, 0.97% (n = 16) are positive for S1-IgG, 0.91% (n = 15) were S1-IgG- borderline and 8.28% (n = 137) exhibit only S1-IgA antibodies. Of the 168 S1-reactive sera, 8.33% (n = 14) have detectable RBD-specific antibodies and 6.55% (n = 11) NCP-specific antibodies. The latter correlates with NTs (kappa coefficient = 0.8660) but start to decline after 3 months. RBD-specific antibodies correlate most closely with the NT (kappa = 0.9448) and only these antibodies are stable for up to six months. All participants with virus-neutralising antibodies report symptoms, of which anosmia and/or dysgeusia correlate most closely with the detection of virus-neutralising antibodies.

Conclusions: RBD-specific antibodies are most reliably detected post-infection, independent of the number/severity of symptoms, and correlate with neutralising antibodies at least for six months. They thus qualify best for large-scale seroepidemiological evaluation of both antibody reactivity and virus neutralisation.

Reference

https://www.nature.com/articles/s43856-021-00012-4

Longitudinal monitoring of laboratory markers characterizes hospitalized and ambulatory COVID-19 patients

Abstract

Early detection of severe forms of COVID-19 is absolutely essential for timely triage of patients. Two well-characterized patient groups were longitudinally followed-up, which were hospitalized moderate to severe (n = 26), and ambulatory mild COVID-19 patients (n = 16) at home quarantine. Human D-dimer, C-reactive protein (CRP), ferritin, cardiac troponin I, interleukin-6 (IL-6) levels were measured on day 1, day 7, day 14 and day 28. All hospitalized patients were SARS-CoV-2 positive on admission, while all ambulatory patients were SARS-CoV-2 positive at recruitment. Hospitalized patients had higher D-dimer, CRP and ferritin, cardiac troponin I and IL-6 levels than ambulatory patients ($p < 0.001$, $p < 0.001$, $p = 0.016$, $p = 0.035$, $p = 0.002$ respectively). Hospitalized patients experienced significant decreases in CRP, ferritin and IL-6 levels from admission to recovery ($p < 0.001$, $p = 0.025$, and $p = 0.001$ respectively). Cardiac troponin I levels were high during the acute phase in both hospitalized and ambulatory patients, indicating a potential myocardial injury. In summary, D-dimer, CRP, ferritin, cardiac troponin I, IL-6 are predictive laboratory markers and can largely determine the clinical course of COVID-19, in particular the prognosis of critically ill COVID-19 patients.

Reference

https://www.nature.com/articles/s41598-021-93950-x

Chronic lung diseases are associated with gene expression programs favoring SARS-CoV-2 entry and severity

Abstract

Patients with chronic lung disease (CLD) have an increased risk for severe coronavirus disease-19 (COVID-19) and poor outcomes. Here, the transcriptomes of 611,398 single cells were analyzed, which were isolated from healthy and CLD lungs to identify molecular characteristics of lung cells that may account for worse COVID-19 outcomes in patients with chronic lung diseases. A similar cellular distribution and relative expression of SARS-CoV-2 entry factors in control and CLD lungs, were observed. CLD

AT2 cells express higher levels of genes linked directly to the efficiency of viral replication and the innate immune response. Additionally, basal differences were identified in inflammatory gene expression programs that highlight how CLD alters the inflammatory microenvironment encountered upon viral exposure to the peripheral lung. The study indicates that CLD is accompanied by changes in cell-type-specific gene expression programs that prime the lung epithelium for and influence the innate and adaptive immune responses to SARS-CoV-2 infection.

Reference

https://www.nature.com/articles/s41467-021-24467-0

Clinical subphenotypes in COVID-19: derivation, validation, prediction, temporal patterns, and interaction with social determinants of health

Abstract

The coronavirus disease 2019 (COVID-19) is heterogeneous and our understanding of the biological mechanisms of host response to the viral infection remains limited. Identification of meaningful clinical subphenotypes may benefit pathophysiological study, clinical practice, and clinical trials. Here, the aim was to derive and validate COVID-19 subphenotypes using machine learning and routinely collected clinical data, assess temporal patterns of these subphenotypes during the pandemic course, and examine their interaction with social determinants of health (SDoH). 14418 COVID-19 patients were retrospectively analyzed in five major medical centers in New York City (NYC), between March 1 and June 12, 2020. Using clustering analysis, 4 biologically distinct subphenotypes were derived in the development cohort (N = 8199). Importantly, the identified subphenotypes were highly predictive of clinical outcomes (especially 60-day mortality). Sensitivity analyses in the development cohort, and rederivation and prediction in the internal (N = 3519) and external (N = 3519) validation cohorts confirmed the reproducibility and usability of the subphenotypes. Further analyses showed varying subphenotype prevalence across the peak of the outbreak in NYC. It was also found that SDoH specifically influenced mortality outcome in Subphenotype IV, which is associated with older age, worse clinical manifestation, and high comorbidity burden. The findings may lead to a better understanding of how COVID-19 causes disease in different populations and potentially benefit clinical trial development. The temporal

patterns and SDoH implications of the subphenotypes may add insights to health policy to reduce social disparity in the pandemic.

Reference

https://www.nature.com/articles/s41746-021-00481-w

The success of SARS-CoV-2 vaccines and challenges ahead

Abstract

The rapid and remarkably successful development, manufacture, and deployment of several effective severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccines is now tempered by three key challenges. First, reducing virus transmission will require prevention of asymptomatic and mild infections in addition to severe symptomatic infections. Second, the emergence of variants of concern with mutations in the S protein's receptor binding domain increases the likelihood that vaccines will have to be updated because some of these mutations render variants less optimally targeted by current vaccines. This will require coordinated global SARS-CoV-2 surveillance to link genotypes to phenotypes, potentially using the WHO's global influenza surveillance program as a guide. Third, concerns about the longevity of vaccine-induced immunity highlight the potential need for re-vaccination, depending on the extent to which the virus has been controlled and whether re-vaccination can target those at greatest risk of severe illness. Fortunately, as I discuss in this review, these challenges can be addressed.

Reference

https://www.cell.com/cell-host-microbe/fulltext/S1931-3128(21)00298-5

SARS-CoV-2 testing and sequencing for international arrivals reveals significant cross border transmission of high risk variants into the United Kingdom

Abstract

Background: Mandatory Day 2 and Day 8 PCR testing and variant sequencing of international arrivals has been recently introduced by the UK Government to mitigate against cross-border transmission of high-risk SARS-CoV-2 variants.

Methods: SARS-CoV-2 testing and sequencing combines TaqPath CE-IVD COVID-19 RT-PCR with Ion AmpliSeq SARS-CoV-2 Next Generation Sequencing Assay. Retrospective analysis of test trending data was performed from initiation of testing on the 11th March through to the 14th April 2021.

Findings: During this time interval, 203,065 SARS-CoV-2 PCR tests were performed, with 3,855 samples testing positive, giving a prevalence of 1.9%. In total 1,913 SARS-CoV-2 genomes were sequenced from positive cases with Ct values < 30 and 1,635 (85.5%) sequences passed quality metrics for lineage analysis. A high diversity of 49 different SARS-CoV-2 variants were identified, including the VOCs B.1.1.7 (Kent; 80.6%), B.1.351 (South Africa; 4.2%), B.1.617.2 (India; 1.7%), P.1 (Brazil; 0.4%) and B.1.1.7 with E484K (Bristol; 0.2%). Vaccine effectiveness was age-related and dose-dependent, ranging from 5% in > 60 with a single dose to 83% in <60 with both doses of a vaccine. Viral load was variant dependent with the B.1.617.2 showing a 21 fold increase in viral copy number compared to the other variants.

Interpretation: The unexpectedly high prevalence of COVID-19 infection in UK arrivals is associated with a rich diversity of SARS-CoV-2 high risk variants entering the UK including the VOC B.1.617.2. Vaccination does not preclude infection and its effectiveness is significantly age-dependent and impacted by variant type. The rapid high-throughput test and sequence workflow we have adopted is particularly suited to the monitoring of cross border transmission and enables immediate public health interventions.

Reference

https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00301-1/fulltext

Oil immersed lossless total analysis system for integrated RNA extraction and detection of SARS-CoV-2

Abstract

The COVID-19 pandemic exposed difficulties in scaling current quantitative PCR (qPCR)-based diagnostic methodologies for large-scale infectious disease testing. Bottlenecks include lengthy multi-step processes for nucleic acid extraction followed by qPCR readouts, which require costly instrumentation and infrastructure, as well as

reagent and plastic consumable shortages stemming from supply chain constraints. Here we report an Oil Immersed Lossless Total Analysis System (OIL-TAS), which integrates RNA extraction and detection onto a single device that is simple, rapid, cost effective, and requires minimal supplies and infrastructure to perform. The performance of OIL-TAS was validated using contrived SARS-CoV-2 viral particle samples and clinical nasopharyngeal swab samples. OIL-TAS showed a 93% positive predictive agreement (n = 57) and 100% negative predictive agreement (n = 10) with clinical SARS-CoV-2 qPCR assays in testing clinical samples, highlighting its potential to be a faster, cheaper, and easier-to-deploy alternative for infectious disease testing.

Reference

https://www.nature.com/articles/s41467-021-24463-4

Theoretical investigation of pre-symptomatic SARS-CoV-2 person-to-person transmission in households

Abstract

Since its emergence, the phenomenon of SARS-CoV-2 transmission by seemingly healthy individuals has become a major challenge in the effort to achieve control of the pandemic. Identifying the modes of transmission that drive this phenomenon is a perquisite in devising effective control measures, but to date it is still under debate. To address this problem, a detailed mathematical model of discrete human actions (such as coughs, sneezes, and touching) was formulated and the continuous decay of the virus in the environment. To take into account those discrete and continuous events we have extended the common modelling approach and employed a hybrid stochastic mathematical framework. This allowed us to calculate higher order statistics, which are crucial for the reconstruction of the observed distributions. Transmission within a household was focused, which was the venue with the highest risk of infection and validated the model results against the observed secondary attack rate and the serial interval distribution. Detailed analysis of the model results identified the dominant driver of pre-symptomatic transmission as the contact route *via* hand-face transfer and showed that wearing masks and avoiding physical contact are an effective prevention strategy. These results provide a sound scientific basis to the present recommendations of the WHO and the CDC.

Reference

https://www.nature.com/articles/s41598-021-93579-w

Publication Date: Jul 13, 2021

COVID-19 mitigation by digital contact tracing and contact prevention (app-based social exposure warnings)

Abstract

A plethora of measures are being combined in the attempt to reduce SARS-CoV-2 spread. Due to its sustainability, contact tracing is one of the most frequently applied interventions worldwide, albeit with mixed results. The performance of digital contact tracing for different infection detection rates and response time delays, was evaluated. a Novel strategy was also introduced and , which was called contact prevention, which emits high exposure warnings to smartphone users according to Bluetooth-based contact counting. We model the effect of both strategies on transmission dynamics in SERIA, an agent-based simulation platform that implements population-dependent statistical distributions. Results show that contact prevention remains effective in scenarios with high diagnostic/response time delays and low infection detection rates, which greatly impair the effect of traditional contact tracing strategies. Contact prevention could play a significant role in pandemic mitigation, especially in developing countries where diagnostic and tracing capabilities are inadequate. Contact prevention could thus sustainably reduce the propagation of respiratory viruses while relying on available technology, respecting data privacy, and most importantly, promoting community-based awareness and social responsibility. Depending on infection detection and app adoption rates, applying a combination of digital contact tracing and contact prevention could reduce pandemic-related mortality by 20–56%.

Reference

https://www.nature.com/articles/s41598-021-93538-5

Reprogrammed CRISPR-Cas13b suppresses SARS-CoV-2 replication and circumvents its mutational escape through mismatch tolerance

Abstract

The recent dramatic appearance of variants of concern of SARS-coronavirus-2 (SARS-CoV-2) highlights the need for innovative approaches that simultaneously suppress viral replication and circumvent viral escape from host immunity and antiviral therapeutics. Here, genome-wide computational prediction and single-nucleotide resolution screening were employed to reprogram CRISPR-Cas13b against SARS-CoV-2 genomic and subgenomic RNAs. Reprogrammed Cas13b effectors targeting accessible regions of Spike and Nucleocapsid transcripts achieved >98% silencing efficiency in virus-free models. Further, optimized and multiplexed Cas13b CRISPR RNAs (crRNAs) suppress viral replication in mammalian cells infected with replication-competent SARS-CoV-2, including the recently emerging dominant variant of concern B.1.1.7. The comprehensive mutagenesis of guide-target interaction demonstrated that single-nucleotide mismatches does not impair the capacity of a potent single crRNA to simultaneously suppress ancestral and mutated SARS-CoV-2 strains in infected mammalian cells, including the Spike D614G mutant. The specificity, efficiency and rapid deployment properties of reprogrammed Cas13b described here provide a molecular blueprint for antiviral drug development to suppress and prevent a wide range of SARS-CoV-2 mutants, and is readily adaptable to other emerging pathogenic viruses.

Reference

https://www.nature.com/articles/s41467-021-24577-9

Placental response to maternal SARS-CoV-2 infection

Abstract

The coronavirus disease 2019 (COVID-19) pandemic affected people at all ages. Whereas pregnant women seemed to have a worse course of disease than age-matched non-pregnant women, the risk of feto-placental infection is low. Using a cohort of 66 COVID-19-positive women in late pregnancy, we correlated clinical parameters with disease severity, placental histopathology, and the expression of viral entry and Interferon-induced transmembrane (IFITM) antiviral transcripts. All newborns were

negative for SARS-CoV-2. None of the demographic parameters or placental histopathological characteristics were associated with disease severity. The fetal-maternal transfer ratio for IgG against the N or S viral proteins was commonly less than one, as recently reported. We found that the expression level of placental ACE2, but not TMPRSS2 or Furin, was higher in women with severe COVID-19. Placental expression of IFITM1 and IFITM3, which have been implicated in antiviral response, was higher in participants with severe disease. We also showed that IFITM3 protein expression, which localized to early and late endosomes, was enhanced in severe COVID-19. Our data suggest an association between disease severity and placental SARS-CoV-2 processing and antiviral pathways, implying a role for these proteins in placental response to SARS-CoV-2.

Reference

https://www.nature.com/articles/s41598-021-93931-0

SARS-CoV-2 test positivity rate in Reno, Nevada: Association with PM2.5 during the 2020 wildfire smoke events in the western United States

Abstract

Background: Air pollution has been linked to increased susceptibility to SARS-CoV-2. Thus, it has been suggested that wildfire smoke events may exacerbate the COVID-19 pandemic.

Objectives: The goal was to examine whether wildfire smoke from the 2020 wildfires in the western United States was associated with an increased rate of SARS-CoV-2 infections in Reno, Nevada.

Methods: A time-series analysis was conducted using generalized additive models to examine the relationship between the SARS-CoV-2 test positivity rate at a large regional hospital in Reno and ambient PM2.5 from 15 May to 20 Oct 2020.

Results: It was found that a 10 $\mu g/m^3$ increase in the 7-day average PM2.5 concentration was associated with a 6.3% relative increase in the SARS-CoV-2 test positivity rate, with a 95% confidence interval (CI) of 2.5 to 10.3%. This corresponded to an estimated 17.7% (CI: 14.4–20.1%) increase in the number of cases during the time period most affected by wildfire smoke, from 16 Aug to 10 Oct.

Significance: Wildfire smoke may have greatly increased the number of COVID-19 cases in Reno. Thus, the results substantiate the role of air pollution in exacerbating the pandemic and can help guide the development of public preparedness policies in areas affected by wildfire smoke, as wildfires are likely to coincide with the COVID-19 pandemic in 2021.

Reference

https://www.nature.com/articles/s41370-021-00366-w

Strand-biased transcription of SARS-CoV-2 and unbalanced inhibition by remdesivir

Abstract

SARS-CoV-2, a positive single-stranded RNA virus, causes the COVID-19 pandemic. During the viral replication and transcription, the RNA dependent RNA polymerase (RdRp) “jumps” along the genome template, resulting in discontinuous negative-stranded transcripts. Although the sense-mRNA architectures of SARS-CoV-2 were reported, its negative strand was unexplored. Here, both strands of RNA were deeply sequenced and found SARS-CoV-2 transcription is strongly biased to form the sense strand with variable transcription efficiency for different genes. During negative strand synthesis, numerous non-canonical fusion transcripts are also formed, driven by 3-15 nt sequence homology scattered along the genome but more prone to be inhibited by SARS-CoV-2 RNA polymerase inhibitor Remdesivir. The drug also represses more of the negative than the positive strand synthesis as supported by a mathematic simulation model and experimental quantifications. Overall, the study opens new sights into SARS-CoV-2 biogenesis and may facilitate the anti-viral vaccine development and drug design.

Reference

https://www.cell.com/iscience/fulltext/S2589-0042(21)00825-7

Integrative resource for network-based investigation of COVID-19 combinatoric drug repositioning and mechanism of action

Abstract

An effective monotherapy to target the complex and multifactorial pathology of SARS-CoV-2 infection poses a challenge to drug repositioning, which can be improved by combination therapy. An online network pharmacology-based drug repositioning platform was developed, COVID-CDR (http://vafaeelab.com/COVID19repositioning.html), that enables a visual and quantitative investigation of the interplay between the drug primary targets and the SARS-CoV-2–host interactome in the human protein-protein interaction network. COVID-CDR prioritizes drug combinations with potential to act synergistically through different, yet potentially complementary pathways. It provides the options for understanding multi-evidence drug-pair similarity scores along with several other relevant information on individual drugs or drug pairs. Overall, COVID-CDR is the first-of-its-kind online platform that provides a systematic approach for pre-clinical in silico investigation of combination therapies for treating COVID-19 at the fingertips of the clinicians and researchers.

Reference

https://www.cell.com/patterns/fulltext/S2666-3899(21)00173-2

An intranasal vaccine durably protects against SARS-CoV-2 variants in mice

Abstract

SARS-CoV-2 variants that attenuate antibody neutralization could jeopardize vaccine efficacy. The protective activity of an intranasally-administered spike protein-based chimpanzee adenovirus-vectored vaccine (ChAd-SARS-CoV-2-S) in animals was recently reported, which has advanced to human trials. Here, its durability, dose-response, and cross-protective activity were assessed in mice. A single intranasal dose of ChAd-SARS-CoV-2-S induced durably high neutralizing and Fc effector antibody responses in serum and S-specific IgG and IgA secreting long-lived plasma cells in the bone marrow. Protection against a historical SARS-CoV-2 strain was observed across a 100-fold vaccine dose range and over a 200-day period. At 6 weeks or 9 months after

vaccination, serum antibodies neutralized SARS-CoV-2 strains with B.1.351, B.1.1.28, and B.1.617.1 spike proteins and conferred almost complete protection in the upper and lower respiratory tracts after challenge with variant viruses. Thus, in mice, intranasal immunization with ChAd-SARS-CoV-2-S provides durable protection against historical and emerging SARS-CoV-2 strains.

Reference

https://www.cell.com/cell-reports/fulltext/S2211-1247(21)00869-X

A SARS-CoV-2 neutralizing antibody selected from COVID-19 patients binds to the ACE2-RBD interface and is tolerant to most known RBD mutations

Abstract

The novel *beta*coronavirus SARS-CoV-2 causes a form of severe pneumonia disease, termed COVID-19. To develop human neutralizing anti-SARS-CoV-2 antibodies, antibody gene libraries from convalescent COVID-19 patients were constructed and recombinant antibody fragments (scFv) against the receptor binding domain (RBD) of the spike protein were selected by phage display. The antibody STE90-C11 shows a sub nM IC_{50} in a plaque-based live SARS-CoV-2 neutralization assay. The in vivo efficacy of the antibody is demonstrated in the Syrian hamster and in the hACE2 mice model. The crystal structure of STE90-C11 Fab in complex with SARS-CoV-2-RBD is solved at 2.0 Å resolution showing that the antibody binds at the same region as ACE2 to RBD. The binding and inhibition of STE90-C11 is not blocked by many known emerging RBD mutations. STE90-C11 derived human IgG1 with FcγR silenced Fc (COR-101) is currently undergoing Phase Ib/II clinical trials for the treatment of moderate to severe COVID-19.

Reference

https://www.cell.com/cell-reports/fulltext/S2211-1247(21)00850-0

Prevention and therapy of SARS-CoV-2 and the B.1.351 variant in mice

Abstract

Improving clinical care for individuals infected with SARS-CoV-2 variants is a global health priority. Small molecule antivirals like remdesivir (RDV) and biologics such as

human monoclonal antibodies (mAb) have demonstrated therapeutic efficacy against SARS-CoV-2, the causative agent of COVID-19. It is not known if combination RDV/mAb will improve outcomes over single agent therapies or whether antibody therapies will remain efficacious against variants. Here, it was shown that a combination of two mAbs in clinical trials, C144 and C135, have potent antiviral effects against even when initiated 48 hours after infection, and have therapeutic efficacy *in vivo* against the B.1.351 variant of concern (VOC). Combining RDV and antibodies provided a modest improvement in outcomes compared to single agents. These data support the continued use of RDV to treat SARS-CoV-2 infections and the continued clinical development of the C144 and C135 antibody combination to treat patients infected with SARS-CoV-2 variants.

Reference

https://www.cell.com/cell-reports/fulltext/S2211-1247(21)00867-6

Social network-based cohorting to reduce the spread of SARS-CoV-2 in secondary schools: A simulation study in classrooms of four European countries

Abstract

Background: Operating schools safely under pandemic conditions is a widespread policy goal. The effectiveness of classroom cohorting, *i.e*., the decomposition of classrooms into smaller isolated units, was analysed in inhibiting the spread of SARS-CoV-2 in European secondary schools and compare different cohorting strategies.

Methods: Using real-world network data on 12,291 adolescents collected in classrooms in England, Germany, the Netherlands, and Sweden in 2010/2011, we apply agent-based simulations to compare the effect of forming cohorts randomly to network-based cohorting. Network-based cohorting attempts to allocate out-of-school contacts to the same cohort to prevent cross-cohort infection more effectively. Explicitly minimizing out-of-school cross-cohort contacts was considered, which is approximating this information-heavy optimization strategy by chained nominations of contacts, and dividing classrooms by gender. The effect of instructing cohorts were compared in-person every second week to daily but separate in-person instruction of both cohorts.

Findings: It was found that cohorting reduces the spread of SARS-CoV-2 in classrooms. Relative to random cohorting, network-based strategies further reduce infections and quarantines when transmission dynamics are strong. In particular, network-based cohorting inhibits superspreading in classrooms. Cohorting that explicitly minimizes cross-cohort contacts is most effective, but approximation based on chained nominations and classroom division by gender also outperform random cohorting. Every-second-week instruction in-person contains outbreaks more effectively than daily in-person instruction of both cohorts.

Interpretation: Cohorting of school classes can curb SARS-CoV-2 outbreaks in the school context. Factoring in out-of-school contacts can achieve a more effective separation of cohorts. Network-based cohorting reduces the risk of outbreaks in schools and can prevent superspreading events.

Reference

https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762(21)00143-5/fulltext

Impact of original, B.1.1.7, and B.1.351/P.1 SARS-CoV-2 lineages on vaccine effectiveness of two doses of COVID-19 mRNA vaccines: Results from a nationwide case-control study in France

Abstract

Background: It was aimed to assess the effectiveness of two doses of mRNA COVID-19 vaccines against COVID-19 with the original virus and other lineages circulating in France.

Methods: In this nationwide case-control study, cases were SARS-CoV-2 infected adults with onset of symptoms between 14 February and 3 May 2021. Controls were non-infected adults from a national representative panel matched to cases by age, sex, region, population density and calendar week. Participants completed an online questionnaire on recent activity-related exposures and vaccination history. Information about the infecting virus was based on a screening RT-PCR for either B.1.1.7 or B.1.351/P.1 variants.

Findings: Included in the analysis were 7 288 adults infected with the original SARS-CoV-2 virus, 31 313 with the B.1.1.7 lineage, 2 550 with B.1.351/P1 lineages, and 3 644

controls. In multivariable analysis, the vaccine effectiveness (95% confidence interval) seven days after the second dose of mRNA vaccine was estimated at 88% (81-92), 86% (81-90) and 77% (63-86) against COVID-19 with the original virus, the B.1.1.7 lineage, and the B.1.351/P.1 lineages, respectively. Recent (2 to 6 months) history of virologically confirmed SARS-CoV-2 infection was found to be 83% (76-88), 88% (85-91) and 83% (71-90) protective against COVID-19 with the original virus, the B.1.1.7 lineage, and the B.1.351/P.1 lineages, respectively; and more distant (> 6 months) infections were 76% (54-87), 84% (75-90), and 74% (41-89) protective against COVID-19 with the original virus, the B.1.1.7 lineage, and the B.1.351/P.1 lineages, respectively.

Interpretation: In real-life settings, two doses of mRNA vaccines proved to be effective against COVID-19 with the original virus, B.1.1.7 lineage and B.1.351/P.1 lineages.

Reference

https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762(21)00148-4/fulltext

Estimating under-recognized COVID-19 deaths, United States, March 2020-May 2021 using an excess mortality modelling approach

Abstract

Background: In the United States, Coronavirus Disease 2019 (COVID-19) deaths are captured through the National Notifiable Disease Surveillance System and death certificates reported to the National Vital Statistics System (NVSS). However, not all COVID-19 deaths are recognized and reported because of limitations in testing, exacerbation of chronic health conditions that are listed as the cause of death, or delays in reporting. Estimating deaths may provide a more comprehensive understanding of total COVID-19–attributable deaths.

Methods: COVID-19 unrecognized attributable deaths were estimated, from March 2020—April 2021, using all-cause deaths reported to NVSS by week and six age groups (0–17, 18–49, 50–64, 65–74, 75–84, and ≥85 years) for 50 states, New York City, and the District of Columbia using a linear time series regression model. Reported COVID-19 deaths were subtracted from all-cause deaths before applying the model. Weekly expected deaths, assuming no SARS-CoV-2 circulation and predicted all-cause

deaths using SARS-CoV-2 weekly percent positive as a covariate were modelled by age group and including state as a random intercept. COVID-19–attributable unrecognized deaths were calculated for each state and age group by subtracting the expected all-cause deaths from the predicted deaths.

Findings: It was estimated that 766,611 deaths attributable to COVID-19 occurred in the United States from March 8, 2020—May 29, 2021. Of these, 184,477 (24%) deaths were not documented on death certificates. Eighty-two percent of unrecognized deaths were among persons aged ≥65 years; the proportion of unrecognized deaths were 0•24–0•31 times lower among those 0–17 years relative to all other age groups. More COVID-19–attributable deaths were not captured during the early months of the pandemic (March–May 2020) and during increases in SARS-CoV-2 activity (July 2020, November 2020—February 2021).

Discussion: Estimating COVID-19–attributable unrecognized deaths provides a better understanding of the COVID-19 mortality burden and may better quantify the severity of the COVID-19 pandemic.

Reference

https://www.thelancet.com/journals/lanam/article/PIIS2667-193X(21)00011-9/fulltext

Phylogenetic estimates of SARS-CoV-2 introductions into Washington State

Abstract

Background: The first confirmed case of SARS-CoV-2 in North America was identified in Washington state on January 21, 2020. We aimed to quantify the number and temporal trends of out-of-state introductions of SARS-CoV-2 into Washington.

Methods: We conducted a molecular epidemiologic analysis of 11,422 publicly available whole genome SARS-CoV-2 sequences from GISAID sampled between December 2019 and September 2020. We used maximum parsimony ancestral state reconstruction methods on time-calibrated phylogenies to enumerate introductions/exports, their likely geographic source (US, non-US, and between eastern and western Washington), and estimated date of introduction. To incorporate phylogenetic uncertainty into our estimates, we conducted 5,000 replicate analyses by generating 25 random time-stratified samples of non-Washington reference sequences,

20 random polytomy resolutions, and 10 random resolutions of the reconstructed ancestral state.

Findings: Minimum 287 introductions (range 244-320) were estimated into Washington and 204 exported lineages (range 188-227) of SARS-CoV-2 out of Washington. Introductions began in mid-January and peaked on March 29, 2020. Lineages with the Spike D614G variant accounted for the majority (88%) of introductions. Overall, 61% (range 55-65%) of introductions into Washington likely originated from a source elsewhere within the US, while the remaining 39% (range 35-45%) likely originated from outside of the US. Intra-state transmission accounted for 65% and 28% of introductions into eastern and western Washington, respectively.

Interpretation: The SARS-CoV-2 epidemic in Washington was continually seeded by a large number of introductions. Our findings highlight the importance of genomic surveillance to monitor for emerging variants due to high levels of inter- and intra-state transmission of SARS-CoV-2.

Reference

https://www.thelancet.com/journals/lanam/article/PIIS2667-193X(21)00010-7/fulltext

A longitudinal study of convergence between Black and White COVID-19 mortality: A county fixed effects approach

Abstract

Background: Non-Hispanic Black populations have suffered much greater per capita COVID-19 mortality than White populations. Previous work has shown that rates of Black and White mortality have converged over time. Understanding of COVID-19 disparities over time is complicated by geographic changes in prevalence, and some prior research has claimed that regional shifts in COVID-19 prevalence may explain the convergence.

Methods: Using county-level COVID-19 mortality data stratified by race, we investigate the trajectory of Black and White per capita mortality from June 2020–January 2021. We use a county fixed-effects model to estimate changes within counties, then extend our models to leverage county-level variation in prevalence to study the effects of prevalence versus time trajectories in mortality disparities.

Findings: Over this period, cumulative mortality rose by 61% and 90% for Black and White populations respectively, decreasing the mortality ratio by 0.4 (25.8%). These trends persisted when a county-level fixed-effects model was applied. Results revealed that county-level changes in prevalence nearly fully explain changes in mortality disparities over time.

Interpretation: Results suggest mechanisms underpinning convergence in Black/White mortality are not driven by fixed county-level characteristics or changes in the regional dispersion of COVID-19, but instead by changes within counties. Further, declines in the Black/White mortality ratio over time appear primarily linked to county-level changes in COVID-19 prevalence rather than other county-level factors that may vary with time. Research into COVID-19 disparities should focus on mechanisms that operate within-counties and are consistent with a prevalence-disparity relationship.

Reference

https://www.thelancet.com/journals/lanam/article/PIIS2667-193X(21)00003-X/fulltext

Impact of COVID-19 on liver transplant recipients–A systematic review and meta-analysis

Abstract

Background: Immunosuppression and comorbidities increase the risk of severe coronavirus disease-2019 (COVID-19) in solid organ transplant (SOT) recipients. The outcomes of COVID-19 in liver transplant (LT) recipients remain unclear. It was aimed to analyse the outcomes of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in LT recipients.

Methods: The electronic databases were searched for articles published from 1 December 2019 to 20 May 2021 with MeSH terms COVID-19, SARS-CoV-2, and liver transplantation. Studies reporting outcomes in more than 10 LT recipients were included for analysis. LT vs non-LT patients with COVID-19 infection were compared for all-cause mortality, which was the primary outcome studied. We also evaluated the relation between the timing of COVID-19 infection post-LT (< one year vs > one year) and mortality.

Findings: Eighteen articles reporting 1,522 COVID-19 infected LT recipients were included for the systematic review. The mean age (standard deviation [SD]) was 60·38 (5·24) years, and 68·5% were men. The mean time (SD) to COVID-19 infection was 5·72 (1·75) years. Based on 17 studies (I2 = 7·34) among 1,481 LT recipients, the cumulative incidence of mortality was 17·4% (95% confidence interval [CI], 15·4–19·6). Mortality was comparable between LT (n = 610) and non-LT (n = 239,704) patients, based on four studies (odds ratio [OR], 0·8 [0·6–1·08]; P = 0·14). Additionally, there was no significant difference in mortality between those infected within one year vs after one year of LT (OR, 1·5 [0·63–3·56]; P = 0·35). The cumulative incidence of graft dysfunction was 2·3% (1·3–4·1). Nearly 23% (20·71–25) of the LT patients developed severe COVID-19 infection. Before infection, 71% and 49% of patients were on tacrolimus and mycophenolate mofetil, respectively. Immunosuppression was modified in 55·9% (38·1–72·2) patients after COVID-19 infection.

Interpretation: LT and non-LT patients with COVID-19 have a similar risk of adverse outcomes.

Reference

https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00305-9/fulltext

Comparing the diagnostic accuracy of point-of-care lateral flow antigen testing for SARS-CoV-2 with RT-PCR in primary care (REAP-2)

Abstract

Background: Testing for COVID-19 with quantitative reverse transcriptase-polymerase chain reaction (RT-PCR) may result in delayed detection of disease. Antigen detection via lateral flow testing (LFT) is faster and amenable to population-wide testing strategies. Our study assesses the diagnostic accuracy of LFT compared to RT-PCR on the same primarycare patients in Austria.

Methods: Patients with mild to moderate flu-like symptoms attending a general practice network in an Austrian district (October 22 to November 30, 2020) received clinical assessment including LFT. All suspected COVID-19 cases obtained additional RT-PCR and were divided into two groups: Group 1 (true reactive): suspected cases with

reactive LFT and positive RT-PCR; and Group 2 (false non-reactive): suspected cases with a non-reactive LFT but positive RT-PCR.

Findings: Of the 2,562 symptomatic patients, 1,037 were suspected of COVID-19 and 826 (79.7%) patients tested RT-PCR positive. Among patients with positive RT-PCR, 788/826 tested LFT reactive (Group 1) and 38 (4.6%) non-reactive (Group 2). Overall sensitivity was 95.4% (95%CI: [94%,96.8%]), specificity 89.1% (95%CI: [86.3%, 91.9%]), positive predictive value 97.3% (95%CI:[95.9%, 98.7%]) and negative predictive value 82.5% (95%CI:[79.8%, 85.2%]). Reactive LFT and positive RT-PCR were positively correlated ($r = 0.968$,95CI=[0.952,0.985] and $\kappa=0.823$, 95%CI=[0.773,0.866]). Reactive LFT was negatively correlated with Ct-value ($r = -0.2999$,$p < 0.001$) and pre-test symptom duration ($r = -0.1299$,$p = 0.0043$) while Ct-value was positively correlated with pre-test symptom duration ($r = 0.3733$),$p < 0.001$).

Interpretation: We show that LFT is an accurate alternative to RT-PCR testing in primary care. We note the importance of administering LFT properly, here combined with clinical assessment in symptomatic patients.

Reference

https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00291-1/fulltext

Comparison of IgG and neutralizing antibody responses after one or two doses of COVID-19 mRNA vaccine in previously infected and uninfected individuals

Abstract

Background: Recent reports have suggested that among individuals previously infected with SARS-CoV-2, a single mRNA vaccine dose is sufficient to elicit high levels of immunity.

Methods: It was compared that anti-SARS-CoV-2 spike receptor binding domain (RBD) IgG antibody concentrations and antibody-mediated neutralization of spike-angiotensin-converting enzyme (ACE2) receptor binding *in vitro* following vaccination of non-hospitalized participants by sero-status and acute virus diagnosis history. Participants were analysed before and after mRNA vaccination (BNT162b2/Pfizer or mRNA-1273/Moderna) in a community-based, home-collected, longitudinal serosurvey in the Chicago area (USA); none reported hospitalization for COVID-19. Samples were

collected in January and February 2021. Before vaccination, some reported prior positive acute viral diagnostic testing and were seropositive (COVID-19+); the others who did not report acute viral diagnostic testing were categorized as seropositive or seronegative based on anti-spike RBD IgG test results.

Findings: Of 307 unique vaccine recipients, 46 reported a prior COVID-19 diagnosis and were seropositive (COVID-19 +). Of the 261 with no history of acute viral diagnostic testing, 117 were seropositive and 144 seronegative before vaccination. The median age was 38 years (range 21–83) with 67 female and 33% male; 40% were non-White. Responses were evaluated after one (n = 142) or two (n = 191) doses of BNT162b2 or mRNA-1273 vaccine. After one dose, median post-vaccine IgG concentration and percent surrogate neutralization were each significantly higher among the COVID-19+ (median 48·2 µg/ml, IgG; > 99.9% neutralization) compared to the seropositives (3·6 µg /ml IgG; 56.5% neutralization) and seronegatives (2·6 µg /ml IgG; 38·3% neutralization). The latter two groups reached > 95% neutralization after the second vaccine dose.

Interpretation: After one dose of mRNA vaccine, individuals previously diagnosed with COVID-19 responded with high levels of anti-RBD IgG and surrogate neutralization of spike-ACE2 interaction. One dose of mRNA vaccine was not sufficient to generate comparably high responses among most persons previously infected with SARS-CoV-2 without a clinical COVID-19 diagnosis, nor among seronegative persons.

Reference

https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00298-4/fulltext

Publication Date: Jul 12, 2021

Deep learning for COVID-19 detection based on CT images

Abstract

COVID-19 has tremendously impacted patients and medical systems globally. Computed tomography images can effectively complement the reverse transcription-polymerase chain reaction testing. This study adopted a convolutional neural network for COVID-19 testing. It was examined that the performance of different pre-trained models on CT testing and identified that larger, out-of-field datasets boost the testing power of the models. This suggests that a priori knowledge of the models from out-of-

field training is also applicable to CT images. The proposed transfer learning approach proves to be more successful than the current approaches described in literature. It was believed that the approach has achieved the state-of-the-art performance in identification thus far. Based on experiments with randomly sampled training datasets, the results reveal a satisfactory performance by the model. It was investigated that the relevant visual characteristics of the CT images used by the model; these may assist clinical doctors in manual screening.

Reference

https://www.nature.com/articles/s41598-021-93832-2

The zinc finger transcription factor, KLF2, protects against COVID-19 associated endothelial dysfunction

Abstract

Coronavirus disease 2019 (COVID-19) is regarded as an endothelial disease (endothelialitis) with its patho-mechanism being incompletely understood. Emerging evidence has demonstrated that endothelial dysfunction precipitates COVID-19 and its accompanying multi-organ injuries. Thus, pharmacotherapies targeting endothelial dysfunction have potential to ameliorate COVID-19 and its cardiovascular complications. The objective of the present study is to evaluate whether kruppel-like factor 2 (KLF2), a master regulator of vascular homeostasis, represents a therapeutic target for COVID-19-induced endothelial dysfunction. Here, it was demonstrated that the expression of KLF2 was reduced and monocyte adhesion was increased in endothelial cells treated with COVID-19 patient serum due to elevated levels of pro-adhesive molecules, ICAM1 and VCAM1. IL-1β and TNF-α, two cytokines elevated in cytokine release syndrome in COVID-19 patients, decreased KLF2 gene expression. Pharmacologic (atorvastatin and tannic acid) and genetic (adenoviral overexpression) approaches to augment KLF2 levels attenuated COVID-19-serum-induced increase in endothelial inflammation and monocyte adhesion. Next-generation RNA-sequencing data showed that atorvastatin treatment leads to a cardiovascular protective transcriptome associated with improved endothelial function (vasodilation, anti-inflammation, antioxidant status, anti-thrombosis/-coagulation, anti-fibrosis, and reduced angiogenesis). Finally, knockdown of KLF2 partially reversed the ameliorative effect of

atorvastatin on COVID-19-serum-induced endothelial inflammation and monocyte adhesion. Collectively, the present study implicates loss of KLF2 as an important molecular event in the development of COVID-19-induced vascular disease and suggests that efforts to augment KLF2 levels may be therapeutically beneficial.

Reference

https://www.nature.com/articles/s41392-021-00690-5

Inferring the ecological niche of bat viruses closely related to SARS-CoV-2 using phylogeographic analyses of *Rhinolophus* species

Abstract

The Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2) is the causal agent of the coronavirus disease 2019 (COVID-19) pandemic. To date, viruses closely related to SARS-CoV-2 have been reported in four bat species: *Rhinolophus acuminatus*, *Rhinolophus affinis*, *Rhinolophus malayanus*, and *Rhinolophus shameli*. Here, we analysed 343 sequences of the mitochondrial cytochrome c oxidase subunit 1 gene (CO1) from georeferenced bats of the four *Rhinolophus* species identified as reservoirs of viruses closely related to SARS-CoV-2. Haplotype networks were constructed in order to investigate patterns of genetic diversity among bat populations of Southeast Asia and China. No strong geographic structure was found for the four Rhinolophus species, suggesting high dispersal capacity. The ecological niche of bat viruses closely related to SARS-CoV-2 was predicted using the four localities in which bat viruses were recently discovered and the localities where bats showed the same CO1 haplotypes than virus-positive bats. The ecological niche of bat viruses related to SARS-CoV was deduced from the localities where bat viruses were previously detected. The results show that the ecological niche of bat viruses related to SARS-CoV2 includes several regions of mainland Southeast Asia whereas the ecological niche of bat viruses related to SARS-CoV is mainly restricted to China. In agreement with these results, human populations in Laos, Vietnam, Cambodia, and Thailand appear to be much less affected by the COVID-19 pandemic than other countries of Southeast Asia. In the climatic transitional zone between the two ecological niches (southern Yunnan, northern Laos, northern Vietnam), genomic recombination between highly divergent viruses is more likely to occur. Considering the limited data and the risk of recombinant

bat-CoVs emergence as the source of new pandemics in humans, the bat populations in these regions should be under surveillance.

Reference

https://www.nature.com/articles/s41598-021-93738-z

Methylene Blue has a potent antiviral activity against SARS-CoV-2 and H1N1 influenza virus in the absence of UV-activation *in vitro*

Abstract

Methylene blue is an FDA (Food and Drug Administration) and EMA (European Medicines Agency) approved drug with an excellent safety profile. It displays broad-spectrum virucidal activity in the presence of UV light and has been shown to be effective in inactivating various viruses in blood products prior to transfusions. In addition, its use has been validated for methemoglobinemia and malaria treatment. In this study, it was first evaluated the virucidal activity of methylene blue against influenza virus H1N1 upon different incubation times and in the presence or absence of light activation, and then against SARS-CoV-2. It was further assessed that the therapeutic activity of methylene blue by administering it to cells previously infected with SARS-CoV-2. Finally, the effect of co-administration of the drug together with immune serum was examined. The findings reveal that methylene blue displays virucidal preventive or therapeutic activity against influenza virus H1N1 and SARS-CoV-2 at low micromolar concentrations and in the absence of UV-activation. It was also confirmed that MB antiviral activity is based on several mechanisms of action as the extent of genomic RNA degradation is higher in presence of light and after long exposure. The work supports the interest of testing methylene blue in clinical studies to confirm a preventive and/or therapeutic efficacy against both influenza virus H1N1 and SARS-CoV-2 infections.

Reference

https://www.nature.com/articles/s41598-021-92481-9

COUnty aggRegation mixup AuGmEntation (COURAGE) COVID-19 prediction

Abstract

The global spread of COVID-19, the disease caused by the novel coronavirus SARS-CoV-2, has casted a significant threat to mankind. As the COVID-19 situation continues to evolve, predicting localized disease severity is crucial for advanced resource allocation. This paper proposes a method named COURAGE (COUnty aggRegation mixup AuGmEntation) to generate a short-term prediction of 2-week-ahead COVID-19 related deaths for each county in the United States, leveraging modern deep learning techniques. Specifically, our method adopts a self-attention model from Natural Language Processing, known as the transformer model, to capture both short-term and long-term dependencies within the time series while enjoying computational efficiency. The model solely utilizes publicly available information for COVID-19 related confirmed cases, deaths, community mobility trends and demographic information, and can produce state-level predictions as an aggregation of the corresponding county-level predictions. The numerical experiments demonstrate that the model achieves the state-of-the-art performance among the publicly available benchmark models.

Reference

https://www.nature.com/articles/s41598-021-93545-6

Deep learning identifies antigenic determinants of severe SARS-CoV-2 infection within T-cell repertoires

Abstract

SARS-CoV-2 infection is characterized by a highly variable clinical course with patients experiencing asymptomatic infection all the way to requiring critical care support. This variation in clinical course has led physicians and scientists to study factors that may predispose certain individuals to more severe clinical presentations in hopes of either identifying these individuals early in their illness or improving their medical management. It was sought to understand immunogenomic differences that may result in varied clinical outcomes through analysis of T-cell receptor sequencing (TCR-Seq) data in the open access ImmuneCODE database. Two cohorts were identified within the database that had clinical outcomes data reflecting severity of illness and utilized

DeepTCR, a multiple-instance deep learning repertoire classifier, to predict patients with severe SARS-CoV-2 infection from their repertoire sequencing. It was demonstrated that patients with severe infection have repertoires with higher T-cell responses associated with SARS-CoV-2 epitopes and identify the epitopes that result in these responses. The results provide evidence that the highly variable clinical course seen in SARS-CoV-2 infection is associated to certain antigen-specific responses.

Reference

https://www.nature.com/articles/s41598-021-93608-8

Publication Date: Jul 10, 2021

Sensor array and gas chromatographic detection of the blood serum volatolomic signature of COVID-19

Abstract

Volatolomics is gaining consideration as a viable approach to diagnose several diseases, and it also shows promising results to discriminate COVID-19 patients via breath analysis. This paper extends the study of the relationship between volatile compounds (VOCs) and COVID-19 to blood serum. Blood samples were collected from subjects recruited at the emergency department of a large public hospital. The volatile compounds (VOCs) were analyzed with a Gas Chromatography Mass Spectrometer (GC/MS). GC/MS data shows that in more than 100 different VOCs, the pattern of abundances of 17 compounds identifies COVID-19 from non-COVID with an accuracy of 89% (sensitivity 94% and specificity 83%). GC/MS analysis was complemented by an array of gas sensors whose data achieved an accuracy of 89% (sensitivity 94% and specificity 80%).

Reference

https://www.cell.com/iscience/fulltext/S2589-0042(21)00819-1

mRNA-1273 COVID-19 vaccine effectiveness against the B.1.1.7 and B.1.351 variants and severe COVID-19 disease in Qatar

Abstract

The SARS-CoV-2 pandemic continues to be a global health concern. The mRNA-1273 (Moderna) vaccine was reported to have an efficacy of 94.1% at preventing symptomatic COVID-19 due to infection with 'wild-type' variants in a randomized clinical trial. Here, the real-world effectiveness of this vaccine were assessed against SARS-CoV-2 variants of concern, specifically B.1.1.7 (Alpha) and B.1.351 (Beta), in Qatar, a population that comprises mainly working-age adults, using a matched test-negative, case-control study design. It was shown that vaccine effectiveness was negligible for 2 weeks after the first dose, but increased rapidly in the third and fourth weeks immediately before administration of a second dose. Effectiveness against B.1.1.7 infection was 88.1% (95% confidence interval (CI): 83.7–91.5%) ≥14 days after the first dose but before the second dose, and was 100% (95% CI: 91.8–100.0%) ≥14 days after the second dose. Analogous effectiveness against B.1.351 infection was 61.3% after the first dose (95% CI: 56.5–65.5%) and 96.4% after the second dose (95% CI: 91.9–98.7%). Effectiveness against any severe, critical or fatal COVID-19 disease due to any SARS-CoV-2 infection (predominantly B.1.1.7 and B.1.351) was 81.6% (95% CI: 71.0–88.8%) and 95.7% (95% CI: 73.4–99.9%) after the first and second dose, respectively. The mRNA-1273 vaccine is highly effective against B.1.1.7 and B.1.351 infections, whether symptomatic or asymptomatic, and against any COVID-19 hospitalization and death, even after a single dose.

Reference

https://www.nature.com/articles/s41591-021-01446-y

Alterations of lipid metabolism provide serologic biomarkers for the detection of asymptomatic versus symptomatic COVID-19 patients

Abstract

COVID-19 pandemic exerts a health care emergency around the world. The illness severity is heterogeneous. It is mostly unknown why some individuals who are positive

for SARS-CoV-2 antibodies stay asymptomatic while others show moderate to severe disease symptoms. Reliable biomarkers for early detection of the disease are urgently needed to attenuate the virus's spread and help make early treatment decisions. Bioactive sphingolipids play a crucial role in the regulation of viral infections and pro-inflammatory responses involved in the severity of COVID-19. However, any roles of sphingolipids in COVID-19 development or detection remain unknown. In this study, lipidomics measurement of serum sphingolipids demonstrated that reduced sphingosine levels are highly associated with the development of symptomatic COVID-19 in the majority (99.24%) SARS-CoV-2-infected patients compared to asymptomatic counterparts. The majority of asymptomatic individuals (73%) exhibited increased acid ceramidase (AC) in their serum, measured by Western blotting, consistent with elevated sphingosine levels compared to SARS-CoV-2 antibody negative controls. AC protein was also reduced in almost all of the symptomatic patients' serum, linked to reduced sphingosine levels, measured in longitudinal acute or convalescent COVID-19 samples. Thus, reduced sphingosine levels provide a sensitive and selective serologic biomarker for the early identification of asymptomatic versus symptomatic COVID-19 patients.

Reference

https://www.nature.com/articles/s41598-021-93857-7

Machine learning application for the prediction of SARS-CoV-2 infection using blood tests and chest radiograph

Abstract

Triaging and prioritising patients for RT-PCR test had been essential in the management of COVID-19 in resource-scarce countries. In this study, machine learning (ML) was applied to the task of detection of SARS-CoV-2 infection using basic laboratory markers. We performed the statistical analysis and trained an ML model on a retrospective cohort of 5148 patients from 24 hospitals in Hong Kong to classify COVID-19 and other aetiology of pneumonia. It was validated the model on three temporal validation sets from different waves of infection in Hong Kong. For predicting SARS-CoV-2 infection, the ML model achieved high AUCs and specificity but low sensitivity in all three validation sets (AUC: 89.9–95.8%; Sensitivity: 55.5–77.8%; Specificity: 91.5–98.3%). When used in adjunction with radiologist interpretations of chest radiographs,

the sensitivity was over 90% while keeping moderate specificity. Our study showed that machine learning model based on readily available laboratory markers could achieve high accuracy in predicting SARS-CoV-2 infection.

Reference

https://www.nature.com/articles/s41598-021-93719-2

Body composition predictors of outcome in patients with COVID-19

Abstract

Background/Objective: Obesity is a strong risk factor for adverse outcomes in patients hospitalized with COVID-19, however, the distribution of fat and the amount of muscle mass are more accurate risk factors than BMI. The objective of this study was to assess body composition measures obtained on opportunistic abdominal CTs as predictors of outcome in patients hospitalized with COVID-19. It was hypothesized that elevated visceral and intermuscular adipose tissue would be associated with adverse outcome.

Subjects/Methods: The retrospective study was IRB-approved and HIPAA-compliant. The study group comprised 124 patients (median age: 68 years, IQR: 56, 77; 59 weeks, 65 months) who were admitted with COVID-19 to a single hospital and who had undergone abdominal CT for clinical purposes. Visceral adipose tissue (VAT), subcutaneous adipose tissue (SAT), intermuscular adipose tissue (IMAT), and paraspinal and abdominal muscle cross-sectional areas (CSA) were assessed. Clinical information including prognostic factors, time of admission to the intensive care unit (ICU) and time of death within 28 days were obtained. Multivariate time-to-event competing risk models were fitted to estimate the hazard ratio (HR) for a composite outcome of ICU admission/mortality associated with a one standard deviation increase in each body compositional measure. Each model was adjusted for age, sex, race, BMI, and cardiometabolic comorbidities.

Results: There were 50 patients who were admitted to the ICU or deceased over a median time of 1 day [IQR 1, 6] from hospital admission. Higher VAT/SAT ratio (HR of 1.30; 95% CI 1.04–1.62, $p = 0.022$) and higher IMAT CSA (HR of 1.44; 95% CI 1.10–1.89, $p = 0.008$) were associated with a reduced time to ICU admission or death in adjusted models.

Conclusion: VAT/SAT and IMAT are predictors of adverse outcome in patients hospitalized with COVID-19, independent of other established prognostic factors. This suggests that body composition measures may serve as novel biomarkers of outcome in patients with COVID-19.

Reference

https://www.nature.com/articles/s41366-021-00907-1

Direct RT-PCR amplification of SARS-CoV-2 from clinical samples using a concentrated viral lysis-amplification buffer prepared with IGEPAL-630

Abstract

The pandemic of 2019 caused by the novel coronavirus (SARS-CoV-2) is still rapidly spreading worldwide. Nucleic acid amplification serves as the gold standard method for confirmation of COVID-19 infection. However, challenges faced for diagnostic laboratories from undeveloped countries includes shortage of kits and supplies to purify viral RNA. Therefore, it is urgent to validate alternative nucleic acid isolation methods for SARS-CoV-2. The results demonstrated that a concentrated viral lysis amplification buffer (vLAB) prepared with the nonionic detergent IGEPAL enables qualitative detection of SARS-CoV-2 by direct Reverse Transcriptase-Polymerase Chain Reaction (dRT-PCR). Furthermore, vLAB was effective in inactivating SARS-CoV-2. Since this method is inexpensive and no RNA purification equipment or additional cDNA synthesis is required, this dRT-PCR with vLAB should be considered as an alternative method for qualitative detection of SARS-CoV-2.

Reference

https://www.nature.com/articles/s41598-021-93333-2

Potent and protective IGHV3-53/3-66 public antibodies and their shared escape mutant on the spike of SARS-CoV-2

Abstract

Neutralizing antibodies (nAbs) to SARS-CoV-2 hold powerful potentials for clinical interventions against COVID-19 disease. However, their common genetic and biologic features remain elusive. Here we interrogate a total of 165 antibodies from eight

COVID-19 patients, and find that potent nAbs from different patients have disproportionally high representation of IGHV3-53/3-66 usage, and therefore termed as public antibodies. Crystal structural comparison of these antibodies reveals they share similar angle of approach to RBD, overlap in buried surface and binding residues on RBD, and have substantial spatial clash with receptor angiotensin-converting enzyme-2 (ACE2) in binding to RBD. Site-directed mutagenesis confirms these common binding features although some minor differences are found. One representative antibody, P5A-3C8, demonstrates extraordinarily protective efficacy in a golden Syrian hamster model against SARS-CoV-2 infection. However, virus escape analysis identifies a single natural mutation in RBD, namely K417N found in B.1.351 variant from South Africa, abolished the neutralizing activity of these public antibodies. The discovery of public antibodies and shared escape mutation highlight the intricate relationship between antibody response and SARS-CoV-2, and provide critical reference for the development of antibody and vaccine strategies to overcome the antigenic variation of SARS-CoV-2.

Reference

https://www.nature.com/articles/s41467-021-24514-w

Multi-Omics analysis of respiratory specimen characterizes baseline molecular determinants which associate with SARS-CoV-2 infection and outcome

Abstract

Rapid diagnosis of SARS-CoV-2 infection still remains a major challenge. A multi-omic approach was adopted to analyze the respiratory specimens of 20 SARS-CoV-2 positive, 20 negative and 15 H1N1 pdm 2009 positive cases. Increased basal level of MX1 (MX Dynamin like GTPase 1) and WARS (Tryptophan--tRNA ligase) correlated with SARS-CoV-2 infection and its outcome. These markers were further validated in 200 suspects. MX1>30pg/ml and WARS>25ng/ml segregated virus positives [AUC=94%CI (0.91-0.97)] and severe patients [AUC>0.85%]. The results show significant induction of immune activation; metabolic reprograming and decrease in oxygen transport, wound healing and others linked proteins and metabolites in COVID-19 patients. Multi-omics profiling correlated with viraemia and segregated asymptomatic COVID-19 patients. Additionally, we identified increased respiratory pathogens

[*Burkholderiales*, *Klebsiella-pneumonia*] and decreased *lactobacillus salivarius* (FDR<0.05) in COVID-19 specimens.

Conclusion: Increased basal MX1 and WARS levels correlates with SARS-CoV-2 infection and could aid in the identification of patient's predisposed to higher severity.

Reference

https://www.cell.com/iscience/fulltext/S2589-0042(21)00791-4

Socioeconomic position and the COVID-19 care cascade from testing to mortality in Switzerland: A population-based analysis

Abstract

Background: The inverse care law states that disadvantaged populations need more health care than advantaged populations but receive less. Gaps in COVID-19-related health care and infection control are not well understood. We aimed to examine inequalities in health in the care cascade from testing for SARS-CoV-2 to COVID-19-related hospitalisation, intensive care unit (ICU) admission, and death in Switzerland, a wealthy country strongly affected by the pandemic.

Methods: Surveillance data reported to the Swiss Federal Office of Public Health from March 1, 2020, to April 16, 2021, and 2018 population data, were analyzed. Residential addresses of notifications were geocoded to identify the Swiss neighbourhood index of socioeconomic position (Swiss-SEP). The index describes 1·27 million small neighbourhoods of approximately 50 households each on the basis of rent per m2, education and occupation of household heads, and crowding. Negative binomial regression models were used to calculate incidence rate ratios (IRRs) with 95% credible intervals (CrIs) of the association between ten groups of the Swiss-SEP index defined by deciles (1=lowest, 10=highest) and outcomes. Models were adjusted for sex, age, canton, and wave of the epidemic (before or after June 8, 2020). Three different denominators were used: the general population, the number of tests, and the number of positive tests.

Findings: Analyses were based on 4 129 636 tests, 609 782 positive tests, 26 143 hospitalisations, 2432 ICU admissions, 9383 deaths, and 8 221 406 residents. Comparing the highest with the lowest Swiss-SEP group and using the general

population as the denominator, more tests were done among people living in neighbourhoods of highest SEP compared with lowest SEP (adjusted IRR 1·18 [95% CrI 1·02–1·36]). Among tested people, test positivity was lower (0·75 [0·69–0·81]) in neighbourhoods of highest SEP than of lowest SEP. Among people testing positive, the adjusted IRR was 0·68 (0·62–0·74) for hospitalisation, was 0·54 (0·43–0·70) for ICU admission, and 0·86 (0·76–0·99) for death. The associations between neighbourhood SEP and outcomes were stronger in younger age groups and we found heterogeneity between areas.

Interpretation: The inverse care law and socioeconomic inequalities were evident in Switzerland during the COVID-19 epidemic. People living in neighbourhoods of low SEP were less likely to be tested but more likely to test positive, be admitted to hospital, or die, compared with those in areas of high SEP. It is essential to continue to monitor testing for SARS-CoV-2, access and uptake of COVID-19 vaccination and outcomes of COVID-19. Governments and health-care systems should address this pandemic of inequality by taking measures to reduce health inequalities in response to the SARS-CoV-2 pandemic.

Reference

https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667(21)00160-2/fulltext

Genomics-informed responses in the elimination of COVID-19 in Victoria, Australia: An observational, genomic epidemiological study

Abstract

Background: A cornerstone of Australia's ability to control COVID-19 has been effective border control with an extensive supervised quarantine programme. However, a rapid recrudescence of COVID-19 was observed in the state of Victoria in June, 2020. It wsa aimed to describe the genomic findings that located the source of this second wave and show the role of genomic epidemiology in the successful elimination of COVID-19 for a second time in Australia.

Methods: In this observational, genomic epidemiological study, we did genomic sequencing of all laboratory-confirmed cases of COVID-19 diagnosed in Victoria, Australia between Jan 25, 2020, and Jan 31, 2021. We did phylogenetic analyses,

genomic cluster discovery, and integrated results with epidemiological data (detailed information on demographics, risk factors, and exposure) collected via interview by the Victorian Government Department of Health. Genomic transmission networks were used to group multiple genomic clusters when epidemiological and genomic data suggested they arose from a single importation event and diversified within Victoria. To identify transmission of emergent lineages between Victoria and other states or territories in Australia, all publicly available SARS-CoV-2 sequences uploaded before Feb 11, 2021, were obtained from the national sequence sharing programme AusTrakka, and epidemiological data were obtained from the submitting laboratories. We did phylodynamic analyses to estimate the growth rate, doubling time, and number of days from the first local infection to the collection of the first sequenced genome for the dominant local cluster, and compared our growth estimates to previously published estimates from a similar growth phase of lineage B.1.1.7 (also known as the Alpha variant) in the UK.

Findings: Between Jan 25, 2020, and Jan 31, 2021, there were 20 451 laboratory-confirmed cases of COVID-19 in Victoria, Australia, of which 15 431 were submitted for sequencing, and 11 711 met all quality control metrics and were included in our analysis. We identified 595 genomic clusters, with a median of five cases per cluster (IQR 2–11). Overall, samples from 11 503 (98·2%) of 11 711 cases clustered with another sample in Victoria, either within a genomic cluster or transmission network. Genomic analysis revealed that 10 426 cases, including 10 416 (98·4%) of 10 584 locally acquired cases, diagnosed during the second wave (between June and October, 2020) were derived from a single incursion from hotel quarantine, with the outbreak lineage (transmission network G, lineage D.2) rapidly detected in other Australian states and territories. Phylodynamic analyses indicated that the epidemic growth rate of the outbreak lineage in Victoria during the initial growth phase (samples collected between June 4 and July 9, 2020; 47·4 putative transmission events, per branch, per year [1/years; 95% credible interval 26·0–85·0]), was similar to that of other reported variants, such as B.1.1.7 in the UK (mean approximately 71·5 1/years). Strict interventions were implemented, and the outbreak lineage has not been detected in Australia since Oct 29, 2020. Subsequent cases represented independent international or interstate introductions, with limited local spread.

Interpretation: The study highlights how rapid escalation of clonal outbreaks can occur from a single incursion. However, strict quarantine measures and decisive public health responses to emergent cases are effective, even with high epidemic growth rates. Real-time genomic surveillance can alter the way in which public health agencies view and respond to COVID-19 outbreaks.

Reference

https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667(21)00133-X/fulltext

Difference in mortality among individuals admitted to hospital with COVID-19 during the first and second waves in South Africa: A cohort study

Abstract

Background: The first wave of COVID-19 in South Africa peaked in July, 2020, and a larger second wave peaked in January, 2021, in which the SARS-CoV-2 501Y.V2 (Beta) lineage predominated. It was aimed to compare in-hospital mortality and other patient characteristics between the first and second waves.

Methods: In this prospective cohort study, data was analyzed from the DATCOV national active surveillance system for COVID-19 admissions to hospital from March 5, 2020, to March 27, 2021. The system contained data from all hospitals in South Africa that have admitted a patient with COVID-19. Incidence risk was used for admission to hospital and determined cutoff dates to define five wave periods: pre-wave 1, wave 1, post-wave 1, wave 2, and post-wave 2. the characteristics of patients with COVID-19 were compared, who were admitted to hospital in wave 1 and wave 2, and risk factors for in-hospital mortality accounting for wave period using random-effect multivariable logistic regression.

Findings: Peak rates of COVID-19 cases, admissions, and in-hospital deaths in the second wave exceeded rates in the first wave: COVID-19 cases, 240·4 cases per 100 000 people vs 136·0 cases per 100 000 people; admissions, 27·9 admissions per 100 000 people vs 16·1 admissions per 100 000 people; deaths, 8·3 deaths per 100 000 people vs 3·6 deaths per 100 000 people. The weekly average growth rate in hospital admissions was 20% in wave 1 and 43% in wave 2 (ratio of growth rate in wave 2 compared with wave 1 was 1·19, 95% CI 1·18–1·20). Compared with the first wave,

individuals admitted to hospital in the second wave were more likely to be age 40–64 years (adjusted odds ratio [aOR] 1·22, 95% CI 1·14–1·31), and older than 65 years (aOR 1·38, 1·25–1·52), compared with younger than 40 years; of Mixed race (aOR 1·21, 1·06–1·38) compared with White race; and admitted in the public sector (aOR 1·65, 1·41–1·92); and less likely to be Black (aOR 0·53, 0·47–0·60) and Indian (aOR 0·77, 0·66–0·91), compared with White; and have a comorbid condition (aOR 0·60, 0·55–0·67). For multivariable analysis, after adjusting for weekly COVID-19 hospital admissions, there was a 31% increased risk of in-hospital mortality in the second wave (aOR 1·31, 95% CI 1·28–1·35). In-hospital case-fatality risk increased from 17·7% in weeks of low admission (<3500 admissions) to 26·9% in weeks of very high admission (>8000 admissions; aOR 1·24, 1·17–1·32).

Interpretation: In South Africa, the second wave was associated with higher incidence of COVID-19, more rapid increase in admissions to hospital, and increased in-hospital mortality. Although some of the increased mortality can be explained by admissions in the second wave being more likely in older individuals, in the public sector, and by the increased health system pressure, a residual increase in mortality of patients admitted to hospital could be related to the new Beta lineage.

Reference

https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(21)00289-8/fulltext

Azithromycin versus standard care in patients with mild-to-moderate COVID-19 (ATOMIC2): An open-label, randomised trial

Abstract

Background: The antibacterial, anti-inflammatory, and antiviral properties of azithromycin suggest therapeutic potential against COVID-19. Randomised data in mild-to-moderate disease are not available. It was assessed whether azithromycin is effective in reducing hospital admission in patients with mild-to-moderate COVID-19.

Methods: This prospective, open-label, randomised superiority trial was done at 19 hospitals in the UK. We enrolled adults aged at least 18 years presenting to hospitals with clinically diagnosed, highly probable or confirmed COVID-19 infection, with fewer than 14 days of symptoms, who were considered suitable for initial ambulatory

management. Patients were randomly assigned (1:1) to azithromycin (500 mg once daily orally for 14 days) plus standard care or to standard care alone. The primary outcome was death or hospital admission from any cause over the 28 days from randomisation. The primary and safety outcomes were assessed according to the intention-to-treat principle. This trial is registered at ClinicalTrials.gov (NCT04381962) and recruitment is closed.

Findings: 298 Participants were enrolled from June 3, 2020, to Jan 29, 2021. Three participants withdrew consent and requested removal of all data, and three further participants withdrew consent after randomisation, thus, the primary outcome was assessed in 292 participants (145 in the azithromycin group and 147 in the standard care group). The mean age of the participants was 45·9 years (SD 14·9). 15 (10%) participants in the azithromycin group and 17 (12%) in the standard care group were admitted to hospital or died during the study (adjusted OR 0·91 [95% CI 0·43–1·92], p=0·80). No serious adverse events were reported.

Interpretation: In patients with mild-to-moderate COVID-19 managed without hospital admission, adding azithromycin to standard care treatment did not reduce the risk of subsequent hospital admission or death. The findings do not support the use of azithromycin in patients with mild-to-moderate COVID-19.

Reference

https://www.nature.com/articles/s41598-021-92851-3

Publication Date: Jul 08, 2021

Discovery of potential imaging and therapeutic targets for severe inflammation in COVID-19 patients

Abstract

The Coronavirus disease 2019 (COVID-19) has been spreading worldwide with rapidly increased number of deaths. Hyperinflammation mediated by dysregulated monocyte/macrophage function is considered to be the key factor that triggers severe illness in COVID-19. However, no specific targeting molecule has been identified for detecting or treating hyperinflammation related to dysregulated macrophages in severe COVID-19. In this study, previously published single-cell RNA-sequencing data of

bronchoalveolar lavage fluid cells from thirteen COVID-19 patients were analyzed with publicly available databases for surface and imageable targets. Immune cell composition according to the severity was estimated with the clustering of gene expression data. Expression levels of imaging target molecules for inflammation were evaluated in macrophage clusters from single-cell RNA-sequencing data. In addition, candidate targetable molecules enriched in severe COVID-19 associated with hyperinflammation were filtered. We found that expression of SLC2A3, which can be imaged by [^{18}F]fluorodeoxyglucose, was higher in macrophages from severe COVID-19 patients. Furthermore, by integrating the surface target and drug-target binding databases with RNA-sequencing data of severe COVID-19, we identified candidate surface and druggable targets including CCR1 and FPR1 for drug delivery as well as molecular imaging. The results provide a resource in the development of specific imaging and therapy for COVID-19-related hyperinflammation.

Reference

https://www.nature.com/articles/s41598-021-93743-2

Fuzzy rank-based fusion of CNN models using Gompertz function for screening COVID-19 CT-scans

Abstract

COVID-19 has crippled the world's healthcare systems, setting back the economy and taking the lives of several people. Although potential vaccines are being tested and supplied around the world, it will take a long time to reach every human being, more so with new variants of the virus emerging, enforcing a lockdown-like situation on parts of the world. Thus, there is a dire need for early and accurate detection of COVID-19 to prevent the spread of the disease, even more. The current gold-standard RT-PCR test is only 71% sensitive and is a laborious test to perform, leading to the incapability of conducting the population-wide screening. To this end, in this paper, we propose an automated COVID-19 detection system that uses CT-scan images of the lungs for classifying the same into COVID and Non-COVID cases. The proposed method applies an ensemble strategy that generates fuzzy ranks of the base classification models using the Gompertz function and fuses the decision scores of the base models adaptively to make the final predictions on the test cases. Three transfer learning-based

convolutional neural network models are used, namely VGG-11, Wide ResNet-50-2, and Inception v3, to generate the decision scores to be fused by the proposed ensemble model. The framework has been evaluated on two publicly available chest CT scan datasets achieving state-of-the-art performance, justifying the reliability of the model. The relevant source codes related to the present work is available in: GitHub.

Reference

https://www.nature.com/articles/s41598-021-93658-y

In vitro **Interleukin-7 treatment partially rescues MAIT cell dysfunction caused by SARS-CoV-2 infection**

Abstract

MAIT cells have been shown to be activated upon several viral infections in a TCR-independent manner by responding to inflammatory cytokines secreted by antigen-presenting cells. Recently, a few studies have shown a similar activation of MAIT cells in response to severe acute respiratory coronavirus 2 (SARS-CoV-2) infection. In this study, we investigate the effect of SARS-CoV-2 infection on the frequency and phenotype of MAIT cells by flow cytometry, and we test in vitro stimulation conditions on the capacity to enhance or rescue the antiviral function of MAIT cells from patients with coronavirus disease 2019 (COVID-19). The study, in agreement with recently published studies, confirmed the decline in MAIT cell frequency of hospitalized donors in comparison to healthy donors. MAIT cells of COVID-19 patients also had lower expression levels of TNF-alpha, perforin and granzyme B upon stimulation with IL-12 + IL-18. 24 h' incubation with IL-7 successfully restored perforin expression levels in COVID-19 patients. Combined, our findings support the growing evidence that SARS-CoV-2 is dysregulating MAIT cells and that IL-7 treatment might improve their function, rendering them more effective in protecting the body against the virus.

Reference

https://www.nature.com/articles/s41598-021-93536-7

Quantifying superspreading for COVID-19 using Poisson mixture distributions

Abstract

The number of secondary cases, i.e. the number of new infections generated by an infectious individual, is an important parameter for the control of infectious diseases. When individual variation in disease transmission is present, like for COVID-19, the distribution of the number of secondary cases is skewed and often modeled using a negative binomial distribution. However, this may not always be the best distribution to describe the underlying transmission process. We propose the use of three other offspring distributions to quantify heterogeneity in transmission, and we assess the possible bias in estimates of the mean and variance of this distribution when the data generating distribution is different from the one used for inference. We also analyze COVID-19 data from Hong Kong, India, and Rwanda, and quantify the proportion of cases responsible for 80% of transmission, p80%, while acknowledging the variation arising from the assumed offspring distribution. In a simulation study, we find that variance estimates may be biased when there is a substantial amount of heterogeneity, and that selection of the most accurate distribution from a set of distributions is important. In addition we find that the number of secondary cases for two of the three COVID-19 datasets is better described by a Poisson-lognormal distribution.

Reference

https://www.nature.com/articles/s41598-021-93578-x

Significance of peripheral blood indexes in differential diagnoses of SARS-CoV-2 and New Bunia virus

Abstract

It was aimed to provide a laboratory basis for differential diagnosis of COVID-19 and severe fever with thrombocytopenia syndrome (SFTS). Clinical data were collected from 32 COVID-19 patients (2019-nCoV group), 31 SFTS patients (SFTS group) and 30 healthy controls (control group). For each group of hospitalized patients, a retrospective analysis was performed on specific indices, including cytokines, T-lymphocyte subsets, routine blood parameters, C-reactive protein (CRP) and procalcitonin (PCT), and receiver operating characteristic (ROC) curves for the indices revealed the differences

among groups. Compared with the 2019-nCoV group, the SFTS group had a significantly and greatly decreased counts of WBC, absolute lymphocyte, PLT and absolute CD4+ T lymphocyte ($P < 0.05$); the IL-6, TNF-α, D-D and PCT levels of the SFTS group were higher than those of the 2019-nCoV group ($P < 0.05$). Compared with those of the SFTS group, the CRP and FIB levels of the 2019-nCoV group were greatly increased ($P < 0.05$). The ROC curves showed that area under the curves (AUCs) for FIB, PLT and TNF-α were greater than 0.85, demonstrating high diagnostic value. At the initial stage of SARS-CoV-2 or SFTS virus infection, PLT, FIB and TNF-α have definitive clinical value for the early and differential diagnosis of these two infections.

Reference

https://www.nature.com/articles/s41598-021-93519-8

Targeting liquid–liquid phase separation of SARS-CoV-2 nucleocapsid protein promotes innate antiviral immunity by elevating MAVS activity

Abstract

Patients with Coronavirus disease 2019 exhibit low expression of interferon-stimulated genes, contributing to a limited antiviral response. Uncovering the underlying mechanism of innate immune suppression and rescuing the innate antiviral response remain urgent issues in the current pandemic. Here it was identified that the dimerization domain of the SARS-CoV-2 nucleocapsid protein (SARS2-NP) is required for SARS2-NP to undergo liquid–liquid phase separation with RNA, which inhibits Lys63-linked poly-ubiquitination and aggregation of MAVS and thereby suppresses the innate antiviral immune response. Mice infected with an RNA virus carrying SARS2-NP exhibited reduced innate immunity, an increased viral load and high morbidity. Notably, we identified SARS2-NP acetylation at Lys375 by host acetyltransferase and reported frequently occurring acetylation-mimicking mutations of Lys375, all of which impaired SARS2-NP liquid–liquid phase separation with RNA. Importantly, a peptide targeting the dimerization domain was screened out to disrupt the SARS2-NP liquid–liquid phase separation and demonstrated to inhibit SARS-CoV-2 replication and rescue innate antiviral immunity both *in vitro* and *in vivo*.

Reference

https://www.nature.com/articles/s41556-021-00710-0

Reduced sensitivity of SARS-CoV-2 variant Delta to antibody neutralization

Abstract

The SARS-CoV-2 B.1.617 lineage was identified in October 2020 in India1–5. It has since then become dominant in some indian regions and UK and further spread to many countries6. The lineage includes three main subtypes (B1.617.1, B.1.617.2 and B.1.617.3), harbouring diverse Spike mutations in the N-terminal domain (NTD) and the receptor binding domain (RBD) which may increase their immune evasion potential. B.1.617.2, also termed variant Delta, is believed to spread faster than other variants. Here, it was isolated an infectious Delta strain from a traveller returning from India. It was examined that its sensitivity to monoclonal antibodies (mAbs) and to antibodies present in sera from COVID-19 convalescent individuals or vaccine recipients, in comparison to other viral strains. Variant Delta was resistant to neutralization by some anti-NTD and anti-RBD mAbs including Bamlanivimab, which were impaired in binding to the Spike. Sera from convalescent patients collected up to 12 months post symptoms were 4 fold less potent against variant Delta, relative to variant Alpha (B.1.1.7). Sera from individuals having received one dose of Pfizer or AstraZeneca vaccines barely inhibited variant Delta. Administration of two doses generated a neutralizing response in 95% of individuals, with titers 3 to 5 fold lower against Delta than Alpha. Thus, variant Delta spread is associated with an escape to antibodies targeting non-RBD and RBD Spike epitopes.

Reference

https://www.nature.com/articles/s41586-021-03777-9

Neutralisation of SARS-CoV-2 lineage P.1 by antibodies elicited through natural SARS-CoV-2 infection or vaccination with an inactivated SARS-CoV-2 vaccine: An immunological study

Abstract

Background: Mutations accrued by SARS-CoV-2 lineage P.1—first detected in Brazil in early January, 2021—include amino acid changes in the receptor-binding domain of the

viral spike protein that also are reported in other variants of concern, including B.1.1.7 and B.1.351. It was aimed to investigate whether isolates of wild-type P.1 lineage SARS-CoV-2 can escape from neutralising antibodies generated by a polyclonal immune response.

Methods: An immunological study was done to assess the neutralising effects of antibodies on lineage P.1 and lineage B isolates of SARS-CoV-2, using plasma samples from patients previously infected with or vaccinated against SARS-CoV-2. Two specimens (P.1/28 and P.1/30) containing SARS-CoV-2 lineage P.1 (as confirmed by viral genome sequencing) were obtained from nasopharyngeal and bronchoalveolar lavage samples collected from patients in Manaus, Brazil, and compared against an isolate of SARS-CoV-2 lineage B (SARS.CoV2/SP02.2020) recovered from a patient in Brazil in February, 2020. Isolates were incubated with plasma samples from 21 blood donors who had previously had COVID-19 and from a total of 53 recipients of the chemically inactivated SARS-CoV-2 vaccine CoronaVac: 18 individuals after receipt of a single dose and an additional 20 individuals (38 in total) after receipt of two doses (collected 17–38 days after the most recent dose); and 15 individuals who received two doses during the phase 3 trial of the vaccine (collected 134–230 days after the second dose). Antibody neutralisation of P.1/28, P.1/30, and B isolates by plasma samples were compared in terms of median virus neutralisation titre (VNT50, defined as the reciprocal value of the sample dilution that showed 50% protection against cytopathic effects).

Findings: In terms of VNT50, plasma from individuals previously infected with SARS-CoV-2 had an 8·6 times lower neutralising capacity against the P.1 isolates (median VNT50 30 [IQR <20–45] for P.1/28 and 30 [<20–40] for P.1/30) than against the lineage B isolate (260 [160–400]), with a binominal model showing significant reductions in lineage P.1 isolates compared with the lineage B isolate ($p \leq 0{\cdot}0001$). Efficient neutralisation of P.1 isolates was not seen with plasma samples collected from individuals vaccinated with a first dose of CoronaVac 20–23 days earlier (VNT50s below the limit of detection [<20] for most plasma samples), a second dose 17–38 days earlier (median VNT50 24 [IQR <20–25] for P.1/28 and 28 [<20–25] for P.1/30), or a second dose 134–260 days earlier (all VNT50s below limit of detection). Median VNT50s against the lineage B isolate were 20 (IQR 20–30) after a first dose of CoronaVac 20–

23 days earlier, 75 (<20–263) after a second dose 17–38 days earlier, and 20 (<20–30) after a second dose 134–260 days earlier. In plasma collected 17–38 days after a second dose of CoronaVac, neutralising capacity against both P.1 isolates was significantly decreased (p=0·0051 for P.1/28 and p=0·0336 for P.1/30) compared with that against the lineage B isolate. All data were corroborated by results obtained through plaque reduction neutralisation tests.

Interpretation: SARS-CoV-2 lineage P.1 might escape neutralisation by antibodies generated in response to polyclonal stimulation against previously circulating variants of SARS-CoV-2. Continuous genomic surveillance of SARS-CoV-2 combined with antibody neutralisation assays could help to guide national immunisation programmes.

Reference

https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247(21)00129-4/fulltext

The effect of methotrexate and targeted immunosuppression on humoral and cellular immune responses to the COVID-19 vaccine BNT162b2: A cohort study

Abstract

Background: Patients on therapeutic immunosuppressants for immune-mediated inflammatory diseases were excluded from COVID-19 vaccine trials. It was therefore aimed to evaluate humoral and cellular immune responses to COVID-19 vaccine BNT162b2 (Pfizer-BioNTech) in patients taking methotrexate and commonly used targeted biological therapies, compared with healthy controls. Given the roll-out of extended interval vaccination programmes to maximise population coverage, we present findings after the first dose.

Methods: In this cohort study, consecutive patients were recruited with a dermatologist-confirmed diagnosis of psoriasis who were receiving methotrexate or targeted biological monotherapy (tumour necrosis factor [TNF] inhibitors, interleukin [IL]-17 inhibitors, or IL-23 inhibitors) from a specialist psoriasis centre serving London and South East England. Consecutive volunteers without psoriasis and not receiving systemic immunosuppression who presented for vaccination at Guy's and St Thomas' NHS Foundation Trust (London, UK) were included as the healthy control cohort. All participants had to be eligible to receive the BNT162b2 vaccine. Immunogenicity was

evaluated immediately before and on day 28 (±2 days) after vaccination. The primary outcomes were humoral immunity to the SARS-CoV-2 spike glycoprotein, defined as neutralising antibody responses to wild-type SARS-CoV-2, and spike-specific T-cell responses (including interferon-γ, IL-2, and IL-21) 28 days after vaccination.

Findings: Between Jan 14 and April 4, 2021, 84 patients with psoriasis (17 on methotrexate, 27 on TNF inhibitors, 15 on IL-17 inhibitors, and 25 on IL-23 inhibitors) and 17 healthy controls were included. The study population had a median age of 43 years (IQR 31–52), with 56 (55%) males, 45 (45%) females, and 85 (84%) participants of White ethnicity. Seroconversion rates were lower in patients receiving immunosuppressants (60 [78%; 95% CI 67–87] of 77) than in controls (17 [100%; 80–100] of 17), with the lowest rate in those receiving methotrexate (seven [47%; 21–73] of 15). Neutralising activity against wild-type SARS-CoV-2 was significantly lower in patients receiving methotrexate (median 50% inhibitory dilution 129 [IQR 40–236]) than in controls (317 [213–487], p=0·0032), but was preserved in those receiving targeted biologics (269 [141–418]). Neutralising titres against the B.1.1.7 variant were similarly low in all participants. Cellular immune responses were induced in all groups, and were not attenuated in patients receiving methotrexate or targeted biologics compared with controls.

Interpretation: Functional humoral immunity to a single dose of BNT162b2 is impaired by methotrexate but not by targeted biologics, whereas cellular responses are preserved. Seroconversion alone might not adequately reflect vaccine immunogenicity in individuals with immune-mediated inflammatory diseases receiving therapeutic immunosuppression. Real-world pharmacovigilance studies will determine how these findings reflect clinical effectiveness.

Reference

https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(21)00212-5/fulltext

Efficacy and safety of an inactivated whole-virion SARS-CoV-2 vaccine (CoronaVac): Interim results of a double-blind, randomised, placebo-controlled, phase 3 trial in Turkey

Abstract

Background: CoronaVac, an inactivated whole-virion SARS-CoV-2 vaccine, has been shown to be well tolerated with a good safety profile in individuals aged 18 years and older in phase 1/2 trials, and provided a good humoral response against SARS-CoV-2. We present the interim efficacy and safety results of a phase 3 clinical trial of CoronaVac in Turkey.

Methods: This was a double-blind, randomised, placebo-controlled phase 3 trial. Volunteers aged 18–59 years with no history of COVID-19 and with negative PCR and antibody test results for SARS-CoV-2 were enrolled at 24 centres in Turkey. Exclusion criteria included (but were not limited to) immunosuppressive therapy (including steroids) within the past 6 months, bleeding disorders, asplenia, and receipt of any blood products or immunoglobulins within the past 3 months. The K1 cohort consisted of health-care workers (randomised in a 1:1 ratio), and individuals other than health-care workers were also recruited into the K2 cohort (randomised in a 2:1 ratio) using an interactive web response system. The study vaccine was 3 μg inactivated SARS-CoV-2 virion adsorbed to aluminium hydroxide in a 0·5 mL aqueous suspension. Participants received either vaccine or placebo (consisting of all vaccine components except inactivated virus) intramuscularly on days 0 and 14. The primary efficacy outcome was the prevention of PCR-confirmed symptomatic COVID-19 at least 14 days after the second dose in the per protocol population. Safety analyses were done in the intention-to-treat population. This study is registered with ClinicalTrials.gov (NCT04582344) and is active but no longer recruiting.

Findings: Among 11 303 volunteers screened between Sept 14, 2020, and Jan 5, 2021, 10 218 were randomly allocated. After exclusion of four participants from the vaccine group because of protocol deviations, the intention-to-treat group consisted of 10 214 participants (6646 [65·1%] in the vaccine group and 3568 [34·9%] in the placebo group) and the per protocol group consisted of 10 029 participants (6559 [65·4%] and 3470 [34·6%]) who received two doses of vaccine or placebo. During a median follow-up

period of 43 days (IQR 36–48), nine cases of PCR-confirmed symptomatic COVID-19 were reported in the vaccine group (31·7 cases [14·6–59·3] per 1000 person-years) and 32 cases were reported in the placebo group (192·3 cases [135·7–261·1] per 1000 person-years) 14 days or more after the second dose, yielding a vaccine efficacy of 83·5% (95% CI 65·4–92·1; p<0·0001). The frequencies of any adverse events were 1259 (18·9%) in the vaccine group and 603 (16·9%) in the placebo group (p=0·0108) with no fatalities or grade 4 adverse events. The most common systemic adverse event was fatigue (546 [8·2%] participants in the vaccine group and 248 [7·0%] the placebo group, p=0·0228). Injection-site pain was the most frequent local adverse event (157 [2·4%] in the vaccine group and 40 [1·1%] in the placebo group, p<0·0001).

Interpretation: CoronaVac has high efficacy against PCR-confirmed symptomatic COVID-19 with a good safety and tolerability profile.

Reference

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)01429-X/fulltext

ROCCA observational study: Early results on safety of Sputnik V vaccine (Gam-COVID-Vac) in the Republic of San Marino using active surveillance

Abstract

Background: In August 2020, Sputnik V was registered as Gam-COVID-Vac by the Russian Ministry of Health, and since December 2020 it has been distributed in 61 countries worldwide. On 25 February 2021, the Republic of San Marino started its vaccination campaign, which includes Sputnik V. The aim was to describe the adverse events following immunization (AEFIs) with this vaccine through participant-based active surveillance in the country.

Methods: Beginning from 4 March to 8 April 2021, a nationwide study was conducted on San Marino's population aged 18–89 years who received one or two doses of Sputnik V. E-questionnaire dissemination occurred through e-mails, QR-codes or live/phone interviews ~7 days after the first and second vaccine dose. A descriptive analysis was conducted to quantify AEFI incidence on both occasions, stratifying results by type and severity of symptoms.

Findings: Mean age of the 2558 vaccine recipients was 66±14 years. First-dose AEFI incidence was 53.3% (systemic reactions at 42.2%), while second-dose AEFI incidence was 66.8% (systemic reactions at 50.4%) (n = 1288). In general, 76.0% of two-dose recipients reported some AEFIs after either vaccine dose, and 2.1% suffered severe reactions; in 60- to 89-year-olds (n = 1021), AEFI incidence was 70.0%, with 53.0% of subjects describing systemic reactions and 0.8% reporting severe symptoms. The most frequent symptoms were local pain, asthenia, headache and joint pain.

Interpretation: The results, albeit preliminary, suggest that Sputnik V has a high tolerability profile in the population aged ≥60 years in terms of short-term AEFIs.

Reference

https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00307-2/fulltext

CORRESPONDANCE

Publication Date: Jul 13, 2021

Antibody response after second BNT162b2 dose in allogeneic HSCT recipients

Uncertainty The prognosis of COVID-19 infection is poor in hematopoietic stem-cell transplant (HSCT) recipients. In a large multicentric series of 318 HSCT recipients (184 allogeneic HSCT recipients and 134 autologous HSCT recipients), the probability of overall survival at 30 days after the diagnosis of COVID-19 infection was notably dismal, at 68% (95% CI 58–77) and 67% (55–78) for allogeneic HSCT recipients and autologous HSCT recipients, respectively. Immunocompromised patients have been excluded from initial studies of SARS-CoV-2 mRNA vaccine efficacy, so the efficacy of vaccination in this population warrants evaluation. To analyse the immunogenicity of the BNT162b2 mRNA vaccine (Pfizer–BioNTech), we used the IgG II Quant Assay (Abbot Laboratories, Wiesbaden, Germany) to quantify spike glycoprotein-specific IgG receptor-binding domain (IgG[S-RBD])levels at a median of 28 days (IQR 26–31) after the second vaccine dose in 88 recipients who had received two successive doses (at 4-week interval) at a median of 23 months (range 3–213 [IQR 9–30]) after allogeneic HSCT. IgG(S-RBD) titres could be quantified in 69 (78%) participants, whereas IgG(S-RBD) was detected but not quantifiable in three participants (anti-S titre <21 arbitrary unit [AU] per mL) and not detected in 16 participants (anti-S titre <6·8 AU/mL). In parallel, nucleoprotein-specific IgG was detected in seven of 88 participants, denoting previous SARS-CoV-2 exposure. For more details, read the link given below.

Reference

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)01594-4/fulltext

NEWS LETTER

Publication Date: Jul 14, 2021

This 'super antibody' for COVID fights off multiple coronaviruses

Scientists have uncovered an antibody that can fight off not only a wide range of SARS-CoV-2 variants, but also closely related coronaviruses. The discovery could aid the quest to develop broad-ranging treatments and vaccines.

Tyler Starr, a biochemist at the Fred Hutchinson Cancer Research Center in Seattle, Washington, and his co-authors set out to shed light on a problem facing antibody treatments for COVID-19: some variants of SARS-CoV-2 have acquired mutations that enable the virus to escape the antibodies' grasp. The researchers examined 12 antibodies isolated from people who had recovered from COVID-19 by Vir Biotechnology, a company based in San Francisco, California, that was involved in the study. Those antibodies latch on to a fragment of viral protein that binds to receptors on human cells. Many antibody therapies for SARS-CoV-2 infection grab the same protein fragment, called the receptor binding domain. One antibody, S2H97, stood out for its capacity to adhere to the binding domains of all the sarbecoviruses that the researchers tested. S2H97, which the authors dub a pan-sarbecovirus antibody, was able to prevent a range of SARS-CoV-2 variants and other sarbecoviruses from spreading among cells growing in the laboratory. It was also powerful enough to protect hamsters against SARS-CoV-2 infection. For more details, read the link given below.

Reference

https://www.nature.com/articles/d41586-021-01917-9

Publication Date: Jul 08, 2021

SARS-CoV-2 targets MAVS for immune evasion

A new study shows that the SARS-CoV-2 nucleocapsid protein represses the antiviral type I interferon response through direct interaction with the signalling adaptor protein

MAVS. Targeting this process might be a useful therapeutic strategy to boost immunity against COVID-19. For more details, read the link given below.

Reference

https://www.nature.com/articles/s41556-021-00712-y

RESOURCES

Publication Date: Jul 10, 2021

SARS-COV-2 spike binding to ACE2 in living cells monitored by TR-FRET

Targeting the interaction between the SARS-CoV-2 spike protein and human ACE2, its primary cell membrane receptor, is a promising therapeutic strategy to prevent viral entry. Recent *in vitro* studies revealed that the receptor binding domain (RBD) of the spike protein plays a prominent role in ACE2 binding, yet a simple and quantitative assay for monitoring this interaction in a cellular environment is lacking. Here, an RBD-ACE2 binding assay was developed that is based on time-resolved FRET, which reliably monitors the interaction in a physiologically relevant and cellular context. Because it is modular, the assay can monitor the impact of different cellular components, such as heparan sulfate, lipids, and membrane proteins on the RBD-ACE2 interaction and it can be extended to the full-length spike protein. The assay is HTS compatible and can detect small-molecule competitive and allosteric modulators of the RBD-ACE2 interaction with high relevance for SARS-CoV-2 therapeutics.

Reference

https://www.cell.com/cell-chemical-biology/fulltext/S2451-9456(21)00307-X

REPORT

Publication Date: Jul 13, 2021

Sputnik V Vaccine Elicits Seroconversion and Neutralizing Capacity to SARS CoV-2 after a Single Dose

Massive vaccination offers great promise for halting the global COVID-19 pandemic. However, limited supply and uneven vaccine distribution create an urgent need to optimize vaccination strategies. SARS-CoV-2-specific antibody responses were evaluated after Sputnik V vaccination of healthcare workers in Argentina, measuring IgG anti-spike titers and neutralizing capacity after one and two doses in a cohort of naïve or previously infected volunteers. By 21 days after receiving the first dose of vaccine, 94% of naïve participants develop spike-specific IgG antibodies. A single Sputnik V dose elicits higher antibody levels and virus neutralizing capacity in previously infected individuals than in naïve ones receiving the full two-dose schedule. The high seroconversion rate after a single dose in naïve participants suggests a benefit of delaying second dose administration to increase the number of people vaccinated. The data presented provide information for guiding public health decisions in light of the current global health emergency.

Reference

https://www.cell.com/cell-reports-medicine/fulltext/S2666-3791(21)00208-1

Publication Date: Jul 09, 2021

Networks of SARS-CoV-2 transmission

The basic reproduction number, R_0 (the number of infections caused by a case in a homogeneously susceptible population), for a particular infection is dependent on the epidemiological triad of the biological characteristics of the pathogen, the environment, and the characteristics of the population. Even for diseases with similar transmission characteristics, R_0 varies by population owing to differential opportunities for onward transmission according to the contact patterns and the size of the transmission network of an infected individual. Although transmission can happen in many settings, some factors facilitate a greater risk of infection because of compounded risks often driven by network dynamics (frequent contacts, close proximity, and prolonged contact) and structural-level determinants (such as poverty, occupation, and household size). Understanding drivers of transmission risks and heterogeneity could be used to improve modeling and guide population- and setting-specific mitigation strategies.

In the context of an epidemic, although each contact carries a risk of acquiring an infection, real-world social networks are complex, often exhibiting extreme heterogeneity in the number of contacts, which have large-scale effects on the spread of infection. In infectious diseases, the population attributable fraction (PAF) represents the total contribution of a risk that could be averted if that risk were avoided. Even for lower-risk exposures, the PAF could increase with higher exposure frequency mediated through greater numbers of contacts. For example, the risk of infection depends on the likelihood of transmission within a particular environment and the frequency at which people visit that setting. At an individual level, settings that are associated with higher-risk factors and visited frequently are likely to pose a higher risk of infection and contribute substantially to cumulative infections than those that may have a higher risk but are visited infrequently. This could mean that a small relative risk of a high-frequency exposure can drive the PAF, suggesting that public health interventions could prioritize resources to eliminate a small risk among many.

However, in reality, risk factors concentrate among the relatively few who have disproportionately higher exposure and onward transmission risks. This individual heterogeneity is evident in data, which consistently indicate higher risks of infection due to higher frequency of exposure and multiple contacts (see the figure). In many countries, those working in low-paid and public-facing jobs had the highest risk of being infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Long-term–care facilities such as nursing homes, homeless shelters, and prisons, as well as workplaces such as meat-packing plants, have been associated with large-scale outbreaks of COVID-19, which were then linked to sustained widespread community transmission. These settings often represent environments where risks for infection are compounded and multiple transmission networks intersect. There is also a clear intersection of COVID-19 risk and socioeconomic inequities, given the network effects of occupation, crowded housing, job insecurity, and poverty. For more details, read the link given below.

Reference

https://science.sciencemag.org/content/373/6551/162

OPINION

Publication Date: Jul 13, 2021

Why are there so few (or so many) circulating coronaviruses?

Despite vast diversity in non-human hosts and conspicuous recent spillover events, only a small number of coronaviruses have been observed to persist in human populations. This puzzling mismatch suggests substantial barriers to establishment. Here, we detail hypotheses that might contribute to explain the low numbers of endemic coronaviruses, despite their considerable evolutionary and emergence potential. The possible explanations were assessed ranging from issues of ascertainment, historically lower opportunities for spillover, aspects of human demographic changes, as well as features of pathogen biology and pre-existing adaptive immunity to related viruses. It was described how successful emergent viral species must triangulate transmission, virulence, and host immunity to maintain circulation. Characterizing factors that might shape the limits of viral persistence can delineate promising research directions to better understand the combinations of pathogens and contexts most likely to lead to spillover.

Reference

https://www.cell.com/trends/immunology/fulltext/S1471-4906(21)00136-8

Publication Date: Jul 14, 2021

Beyond neutralization for BNT162b2 mRNA vaccination

Mounting a robust immune response against SARS-CoV-2 requires neutralization as well as effector T cell functions. In this issue of Cell Host Microbe, Tauzin *et al*. characterize the humoral and T cell responses after a single dose of BNT162b2 mRNA vaccine in individuals with or without previous exposure to SARS-CoV-2. For more details, read the link given below.

Reference

https://www.cell.com/cell-host-microbe/fulltext/S1931-3128(21)00295-X

Publication Date: Jul 08, 2021

Immune responses to COVID-19 vaccines in patients with cancer: Promising results and a note of caution

SARS-CoV-2 vaccines are effective in preventing COVID-19. Patients with cancer are at high risk for severe COVID-19 and are appropriately prioritized for vaccination. Several studies in this issue of Cancer Cell add to our knowledge of the heterogeneity of immune responses to vaccination among patients with cancer and identify important areas for future research. For more details, read the link given below.

Reference

https://www.cell.com/cancer-cell/fulltext/S1535-6108(21)00342-1