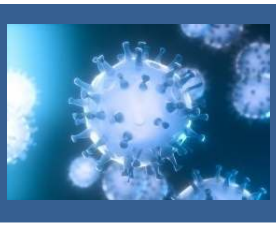
COVID-19

May 27 – Jun 02, 2021



RESEARCH PUBLICATIONS

Publication Date: Jun 02, 2021

Increased extravascular lung water index (EVLWI) reflects rapid non-cardiogenic oedema and mortality in COVID-19 associated ARDS

Abstract

Nearly 5% of patients suffering from COVID-19 develop acute respiratory distress syndrome (ARDS). Extravascular lung water index (EVLWI) is a marker of pulmonary oedema which is associated with mortality in ARDS. In this study, we evaluate whether EVLWI is higher in patients with COVID-19 associated ARDS as compared to COVID-19 negative, ventilated patients with ARDS and whether EVLWI has the potential to monitor disease progression. EVLWI and cardiac function were monitored by transpulmonary thermodilution in 25 patients with COVID-19 ARDS subsequent to intubation and compared to a control group of 49 non-COVID-19 ARDS patients. At intubation, EVLWI was noticeably elevated and significantly higher in COVID-19 patients than in the control group (17 (11–38) vs. 11 (6–26) mL/kg; $p < 0.001$). High pulmonary vascular permeability index values (2.9 (1.0–5.2) versus 1.9 (1.0–5.2); $p = 0.003$) suggested a non-cardiogenic pulmonary oedema. By contrast, the cardiac parameters SVI, GEF and GEDVI were comparable in both cohorts. High EVLWI values were associated with viral persistence, prolonged intensive care treatment and in-hospital mortality ($23.2 \pm 6.7\%$ vs. $30.3 \pm 6.0\%$, $p = 0.025$). Also, EVLWI showed a significant between-subjects ($r = -0.60$; $p = 0.001$) and within-subjects correlation ($r = -0.27$; $p = 0.028$) to Horowitz index. Compared to non COVID-19 ARDS, COVID-19 results in markedly elevated EVLWI-values in patients with ARDS. High EVLWI reflects a non-cardiogenic pulmonary oedema in COVID-19 ARDS and could serve as parameter to monitor ARDS progression on ICU.

Reference

https://www.nature.com/articles/s41598-021-91043-3

A metal ion orients SARS-CoV-2 mRNA to ensure accurate 2′-O methylation of its first nucleotide

Abstract

The SARS-CoV-2 nsp16/nsp10 enzyme complex modifies the 2′-OH of the first transcribed nucleotide of the viral mRNA by covalently attaching a methyl group to it. The 2′-O methylation of the first nucleotide converts the status of mRNA cap from Cap-0 to Cap-1, and thus, helps the virus evade immune surveillance in host cells. Here, we report two structures of nsp16/nsp10 representing pre- and post-release states of the RNA product (Cap-1). We observe overall widening of the enzyme upon product formation, and an inward twisting motion in the substrate binding region upon product release. These conformational changes reset the enzyme for the next round of catalysis. The structures also identify a unique binding mode and the importance of a divalent metal ion for 2′-O methylation. We also describe underlying structural basis for the perturbed enzymatic activity of a clinical variant of SARS-CoV-2, and a previous SARS-CoV outbreak strain.

Reference

https://www.nature.com/articles/s41467-021-23594-y

Study on the prognosis predictive model of COVID-19 patients based on CT radiomics

Abstract

Making timely assessments of disease progression in patients with COVID-19 could help offer the best personalized treatment. The purpose of this study was to explore an effective model to predict the outcome of patients with COVID-19. We retrospectively included 188 patients (124 in the training set and 64 in the test set) diagnosed with COVID-19. Patients were divided into aggravation and improvement groups according to the disease progression. Three kinds of models were established, including the radiomics, clinical, and combined model. Receiver operating characteristic curves, decision curves, and Delong's test were used to evaluate and compare the models. Our

analysis showed that all the established prediction models had good predictive performance in predicting the progress and outcome of COVID-19.

Reference

https://www.nature.com/articles/s41598-021-90991-0

Covid-19 diagnosis by combining RT-PCR and pseudo-convolutional machines to characterize virus sequences

Abstract

The Covid-19 pandemic, a disease transmitted by the SARS-CoV-2 virus, has already caused the infection of more than 120 million people, of which 70 million have been recovered, while 3 million people have died. The high speed of infection has led to the rapid depletion of public health resources in most countries. RT-PCR is Covid-19's reference diagnostic method. In this work we propose a new technique for representing DNA sequences: They are divided into smaller sequences with overlap in a pseudo-convolutional approach and represented by co-occurrence matrices. This technique eliminates multiple sequence alignment. Through the proposed method, it is possible to identify virus sequences from a large database: 347,363 virus DNA sequences from 24 virus families and SARS-CoV-2. When comparing SARS-CoV-2 with virus families with similar symptoms, we obtained 0.97±0.03 for sensitivity and 0.9919±0.0005 for specificity with MLP classifier and 30% overlap. When SARS-CoV-2 is compared to other coronaviruses and healthy human DNA sequences, we obtained 0.99±0.01 for sensitivity and 0.9986±0.0002 for specificity with MLP and 50% overlap. Therefore, the molecular diagnosis of Covid-19 can be optimized by combining RT-PCR and our pseudo-convolutional method to identify DNA sequences for SARS-CoV-2 with greater specificity and sensitivity.

Reference

https://www.nature.com/articles/s41598-021-90766-7

COVID-19 transmission in group living environments and households

Abstract

The coronavirus disease 2019 (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is currently the world's largest public health concern. This study evaluated COVID-19 transmission risks in people in group living environments. A total of 4550 individuals with a history of recent contact with patients at different places (dormitory/home/outside the residences) and levels (close/lower-risk) were tested for SARS-CoV-2 viral RNA using a nasopharyngeal swab test between July 2020 and May 2021. The test-positive rate was highest in individuals who had contact in dormitories (27.5%), but the rates were largely different between dormitories with different infrastructural or lifestyle features and infection control measures among residents. With appropriate infection control measures, the secondary transmission risk in dormitories was adequately suppressed. The household transmission rate (12.6%) was as high as that of close contact outside the residences (11.3%) and accounted for > 60% of the current rate of COVID-19 transmission among non-adults. Household transmission rates synchronized to local epidemics with changed local capacity of quarantining infectious patients. In conclusion, a group living environment is a significant risk factor of secondary transmission. Appropriate infection control measures and quarantine of infectious residents will decrease the risk of secondary transmission in group living environments.

Reference

https://www.nature.com/articles/s41598-021-91220-4

Publication Date: Jun 01, 2021

Real-time, selective, and low-cost detection of trace level SARS-CoV-2 spike-protein for cold-chain food quarantine

Abstract

Due to the friendly temperature for virus survival, SARS-CoV-2 is frequently found in cold-chain foods, posing a serious threat to public health. Utilizing an interdigitated microelectrode chip modified with an antibody probe and integrating dielectrophoresis enrichment with interfacial capacitance sensing, a strategy is presented for the

detection of trace level spike-protein from SARS-CoV-2. It achieves a limit of detection as low as 2.29 × 10−6 ng/mL in 20 s, with a wide linear range of 10−5–10−1 ng/mL and a selectivity of 234:1. The cost for a single test can be controlled to ~1 dollar. This strategy provides a competitive solution for real-time, sensitive, selective, and large-scale application in cold-chain food quarantine.

Reference

https://www.nature.com/articles/s41538-021-00094-3

SARS-CoV-2 variants, spike mutations and immune escape

Abstract

Although most mutations in the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) genome, are expected to be either deleterious and swiftly purged or relatively neutral, a small proportion will affect functional properties and may alter infectivity, disease severity or interactions with host immunity. The emergence of SARS-CoV-2 in late 2019 was followed by a period of relative evolutionary stasis lasting about 11 months. Since late 2020, however, SARS-CoV-2 evolution has been characterized by the emergence of sets of mutations, in the context of ‘variants of concern’, that impact virus characteristics, including transmissibility and antigenicity, probably in response to the changing immune profile of the human population. There is emerging evidence of reduced neutralization of some SARS-CoV-2 variants by postvaccination serum; however, a greater understanding of correlates of protection is required to evaluate how this may impact vaccine effectiveness. Nonetheless, manufacturers are preparing platforms for a possible update of vaccine sequences, and it is crucial that surveillance of genetic and antigenic changes in the global virus population is done alongside experiments to elucidate the phenotypic impacts of mutations. In this Review, the literature on mutations of the SARS-CoV-2 spike protein was summarized, the primary antigen, focusing on their impacts on antigenicity and contextualizing them in the protein structure, and discuss them in the context of observed mutation frequencies in global sequence datasets.

Reference

https://www.nature.com/articles/s41579-021-00573-0

Targeting of the CD80/86 proinflammatory axis as a therapeutic strategy to prevent severe COVID-19

Abstract

An excessive immune response known as cytokine storm is the hallmark of severe COVID-19. The cause of this cytokine rampage is yet not known. Based on recent epidemiological evidence, we hypothesized that CD80/86 signaling is essential for this hyperinflammation, and that blocking this proinflammatory axis could be an effective therapeutic approach to protect against severe COVID-19. Here exploratory evidence was provided that abatacept, a drug that blocks CD80/86 co-stimulation, produces changes at the systemic level that are highly antagonistic of the proinflammatory processes elicited by COVID-19. Using RNA-seq from blood samples from a longitudinal cohort of n = 38 rheumatic patients treated with abatacept, we determined the immunological processes that are significantly regulated by this treatment. We then analyzed available blood RNA-seq from two COVID19 patient cohorts, a very early cohort from the epicenter of the pandemic in China (n = 3 COVID-19 cases and n = 3 controls), and a recent and larger cohort from the USA (n = 49 severe and n = 51 mild COVD-19 patients). We found a highly significant antagonism between SARS-CoV-2 infection and COVID-19 severity with the systemic response to abatacept. Analysis of previous single-cell RNA-seq data from bronchoalveolar lavage fluid from mild and severe COVID-19 patients and controls, reinforce the implication of the CD80/86 proinflammatory axis. Our functional results further support abatacept as a candidate therapeutic approach to prevent severe COVID-19.

Reference

https://www.nature.com/articles/s41598-021-90797-0

Characterization of SARS-CoV-2 nucleocapsid protein reveals multiple functional consequences of the C-terminal domain

Abstract

Nucleocapsid (N) encoded by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) plays key roles in the replication cycle and is a critical serological marker. Here, essential biochemical properties of N were characterized and the utility of these insights

in serological studies was described. *N* Domains were defined, which were important for oligomerization and RNA binding and show that N oligomerization provides a high-affinity RNA-binding platform. We also map the RNA-binding interface, showing protection in the N-terminal domain and linker region. In addition, phosphorylation causes reduction of RNA binding and redistribution of N from liquid droplets to loose coils, showing how N-RNA accessibility and assembly may be regulated by phosphorylation. Finally, it was fond that the C-terminal domain of N is the most immunogenic, based on antibody binding to patient samples. Together, we provide a biochemical description of SARS-CoV-2 N and highlight the value of using N domains as highly specific and sensitive diagnostic markers.

Reference

https://www.cell.com/iscience/fulltext/S2589-0042(21)00649-0

Publication Date: May 31, 2021

Land-use change and the livestock revolution increase the risk of zoonotic coronavirus transmission from rhinolophid bats

Abstract

The extent to which humans facilitate zoonotic transmission of infectious diseases is unclear. Human encroachment into wildlife habitats as a consequence of expanding urbanization, cropland area and intensive animal farming is hypothesized to favour the emergence of zoonotic diseases. Here comprehensive, high-resolution datasets on forest cover, cropland distribution, livestock density, human population, human settlements, bat species' distribution and land-use changes was analysed in regions populated by Asian horseshoe bats (>28.5 million km2)—the species that most commonly carry severe acute respiratory syndrome (SARS)-related coronaviruses. Areas at risk of SARS-related coronavirus outbreaks were identified, showing that areas in China populated by horseshoe bats exhibit higher forest fragmentation and concentrations of livestock and humans than other countries. The findings indicate that human–livestock–wildlife interactions in China may form hotspots with the potential to increase SARS-related coronavirus transmission from animals to humans.

Reference

https://www.nature.com/articles/s43016-021-00285-x

A core-shell structured COVID-19 mRNA vaccine with favorable biodistribution pattern and promising immunity

Abstract

Although inoculation of COVID-19 vaccines has rolled out globally, there is still a critical need for safe and effective vaccines to ensure fair and equitable supply for all countries. Here, we report on the development of a highly efficacious mRNA vaccine, SW0123 that is composed of sequence-modified mRNA encoding the full-length SARS-CoV-2 Spike protein packaged in core–shell structured lipopolyplex (LPP) nanoparticles. SW0123 is easy to produce using a large-scale microfluidics-based apparatus. The unique core–shell structured nanoparticle facilitates vaccine uptake and demonstrates a high colloidal stability, and a desirable biodistribution pattern with low liver targeting effect upon intramuscular administration. Extensive evaluations in mice and nonhuman primates revealed strong immunogenicity of SW0123, represented by induction of Th1-polarized T cell responses and high levels of antibodies that were capable of neutralizing not only the wild-type SARS-CoV-2, but also a panel of variants including D614G and N501Y variants. In addition, SW0123 conferred effective protection in both mice and non-human primates upon SARS-CoV-2 challenge. Taken together, SW0123 is a promising vaccine candidate that holds prospects for further evaluation in humans.

Reference

https://www.nature.com/articles/s41392-021-00634-z

Prophylactic heparin and risk of orotracheal intubation or death in patients with mild or moderate COVID-19 pneumonia

Abstract

Prophylactic low molecular weight heparin (pLMWH) is currently recommended in COVID-19 to reduce the risk of coagulopathy. The aim of this study was to evaluate whether the antinflammatory effects of pLMWH could translate in lower rate of clinical progression in patients with COVID-19 pneumonia. Patients admitted to a COVID-hospital in Rome with SARS-CoV-2 infection and mild/moderate pneumonia were

retrospectively evaluated. The primary endpoint was the time from hospital admission to orotracheal intubation/death (OTI/death). A total of 449 patients were included: 39% female, median age 63 (IQR, 50–77) years. The estimated probability of OTI/death for patients receiving pLMWH was: 9.5% (95% CI 3.2–26.4) by day 20 in those not receiving pLMWH vs. 10.4% (6.7–15.9) in those exposed to pLMWH; p-value = 0.144. This risk associated with the use of pLMWH appeared to vary by PaO2/FiO2 ratio: aHR 1.40 (95% CI 0.51–3.79) for patients with an admission PaO2/FiO2 ≤ 300 mmHg and 0.27 (0.03–2.18) for those with PaO2/FiO2 > 300 mmHg; p-value at interaction test 0.16. pLMWH does not seem to reduce the risk of OTI/death mild/moderate COVID-19 pneumonia, especially when respiratory function had already significantly deteriorated. Data from clinical trials comparing the effect of prophylactic vs. therapeutic dosage of LMWH at various stages of COVID-19 disease are needed.

Reference

https://www.nature.com/articles/s41598-021-90713-6

Are adipokines the missing link between obesity, immune response, and outcomes in severe COVID-19?

Abstract

Introduction: Obesity is commonly reported in COVID-19 patients and is associated with poorer outcomes. It is suggested that leptin could be the missing link between obesity and severe COVID-19. Our study aimed to unravel the link between adipokines, COVID-19 status, immune response, and outcomes in severe pneumonia.

Methods: In this prospective observational single-center study, 63 immunocompetent patients with severe pneumonia (36 non-COVID-19 and 27 COVID-19) were enrolled, most required intensive care. Clinical and biological characteristics (glucose metabolism, plasma adipokines, and cytokine concentrations) and outcomes were compared.

Results: At similar baseline severity, COVID-19 patients required mechanical ventilation for significantly longer than non-COVID-19 patients (p = 0.0049). Plasma concentrations of leptin and adiponectin were respectively positively and negatively correlated with BMI and glucose metabolism (glycemia and insulinemia), but not significantly different

between the two groups. Leptin levels were negatively correlated with IL-1β and IL-6, but the adipokines were not correlated with most other inflammatory mediators, baseline severity (SOFA score), or the duration of mechanical ventilation.

Conclusion: Adipokine levels were correlated with BMI but not with most inflammatory mediators, severity, or outcomes in severe pneumonia, regardless of the origin. The link between obesity, dysregulated immune response, and life-threatening COVID-19 requires further investigation.

Reference

https://www.nature.com/articles/s41366-021-00868-5

AI for radiographic COVID-19 detection selects shortcuts over signal

Abstract

Artificial intelligence (AI) researchers and radiologists have recently reported AI systems that accurately detect COVID-19 in chest radiographs. However, the robustness of these systems remains unclear. Using state-of-the-art techniques in explainable AI, we demonstrate that recent deep learning systems to detect COVID-19 from chest radiographs rely on confounding factors rather than medical pathology, creating an alarming situation in which the systems appear accurate, but fail when tested in new hospitals. It was observed that the approach to obtain training data for these AI systems introduces a nearly ideal scenario for AI to learn these spurious ‘shortcuts’. Because this approach to data collection has also been used to obtain training data for the detection of COVID-19 in computed tomography scans and for medical imaging tasks related to other diseases, the study reveals a far-reaching problem in medical-imaging AI. In addition, we show that evaluation of a model on external data is insufficient to ensure AI systems rely on medically relevant pathology, because the undesired ‘shortcuts’ learned by AI systems may not impair performance in new hospitals. These findings demonstrate that explainable AI should be seen as a prerequisite to clinical deployment of machine-learning healthcare models.

Reference

https://www.nature.com/articles/s42256-021-00338-7

Low-dose Ad26.COV2.S protection against SARS-CoV-2 challenge in rhesus macaques

Abstract

It was previously reported that a single immunization with an adenovirus serotype 26 (Ad26)-vector-based vaccine expressing an optimized SARS-CoV-2 spike (Ad26.COV2.S) protected rhesus macaques against SARS-CoV-2 challenge. To evaluate reduced doses of Ad26.COV2.S, 30 rhesus macaques were immunized once with 1 × 1011, 5 × 1010, 1.125 × 1010, or 2 × 109 viral particles (vp) Ad26.COV2.S or sham and were challenged with SARS-CoV-2. Vaccine doses as low as 2 × 109 vp provided robust protection in bronchoalveolar lavage, whereas doses of 1.125 × 1010 vp were required for protection in nasal swabs. Activated memory B cells and binding or neutralizing antibody titers following vaccination correlated with protective efficacy. At suboptimal vaccine doses, viral breakthrough was observed but did not show enhancement of disease. These data demonstrate that a single immunization with relatively low dose of Ad26.COV2.S effectively protected against SARS-CoV-2 challenge in rhesus macaques, although a higher vaccine dose may be required for protection in the upper respiratory tract.

Reference

https://www.cell.com/cell/fulltext/S0092-8674(21)00693-0

Publication Date: May 30, 2021

Association between previous infection with SARS CoV-2 and the risk of self-reported symptoms after mRNA BNT162b2 vaccination: Data from 3,078 health care workers

Abstract

Background: Health care workers (HCWs) are at high risk of contracting an infection by SARS CoV-2 and thus they are a priority for vaccination. It was hereby aimed to investigate whether the risk of severe and moderate systemic symptoms (MSS) after vaccination is higher in HCWs with a history of previous COVID-19.

Methods: An online questionnaire was offered to the cohort all HCWs undergoing anti-SARS CoV-2 mRNA BNT162b2 vaccination between January 4th and February 9th 2021 in two large tertiary hospitals (ASST Santi Paolo and Carlo) in Milan, Italy. Previous SARS-CoV-2 infection/COVID-19 was recorded. Local and systemic symptoms after each of the two doses were reported. MSS were those either interfering with daily activities or resulting in time off-work. Factors associated to MSS were identified by logistic regression.

Findings: 3,078 HCW were included. Previous SARS-CoV-2 infection/COVID-19 occurred in 396 subjects (12·9%). 59·6% suffered from ≥1 local or systemic symptom after the first and 73·4% after the second dose. MSS occurred in 6·3% of cases (14·4% with previous vs 5·1% with no COVID-19 p<0·001) and in 28·3% (24·5% in COVID-19 vs 28·3% no COVID, p = 0·074) after the first and second dose, respectively. Subjects already experiencing COVID-19 had an independent 3-fold higher risk of MSS after the first and a 30% lower risk after the second dose. No severe adverse events were reported.

Interpretation: The data confirm in a real-world setting, the lack of severe adverse events and the short duration of reactogenicity in already infected HCWs. Possible differences in immune reactivity are drivers of MSS among this group of HCWs, as well as among females and younger individuals.

Reference

https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00194-2/fulltext

Ephrin-A1 and the sheddase ADAM12 are upregulated in COVID-19

Abstract

More than 3.5 million people have died globally from COVID-19, yet an effective therapy is not available. It is, therefore, important to understand the signaling pathways that mediate disease progression in order to identify new molecular targets for therapeutic development. Here, we report that the blood serum levels of ephrin-A1 and the sheddase ADAM12 were significantly elevated in COVID-19 patients treated at SUNY Downstate Hospital of Brooklyn, New York. Both ephrin-A1 and ADAM12 are known to be involved in inflammation and regulate endothelial cell permeability, thus providing a

gateway to lung injury. The clinical outcome correlated with the ephrin-A1 and ADAM12 serum levels during the first week of hospitalization. In contrast, the serum levels of TNFα were elevated in only a small subset of the patients, and these same patients also had highly elevated levels of the sheddase ADAM17. These data indicate that ephrin-A1-mediated inflammatory signaling may contribute to COVID-19 disease progression more so than TNFα-mediated inflammatory signaling. They also support the notion that, in COVID-19 inflammation, ADAM12 sheds ephrin-A1, while ADAM17 sheds TNFα. Furthermore, the results suggest that elevated serum levels and activity of cytokines, such as TNFα, and other secreted inflammatory molecules, such as ephrin-A1, are not simply due to overexpression, but also to upregulation of sheddases that release them into the blood circulation. The results identify ephrin-A1, ADAM12, and other molecules in the ephrin-A1 signaling pathway as potential pharmacological targets for treating COVID-19 inflammation.

Reference

https://www.cell.com/heliyon/fulltext/S2405-8440(21)01303-7

Using SNSs for early detection of disease outbreak in developing countries: Evidence from COVID-19 pandemic in Nigeria

Abstract

Developing countries, particularly Nigeria, continually find it challenging to proactively and actively carry out early-stage surveillance for disease outbreaks due to the lack of quality workforce, a dearth of public health data, and the absence of automated surveillance systems in the country. This study presents the potential and ability of Twitter in tracking early detection of COVID-19, monitoring the dissemination of information, and exploration of public awareness and attitudes among Nigerians. Tweets mentioning COVID-19 and related keywords were collected in 11 batches via the NCapture™ plugin available on Google Chrome from February 20 - May 6, 2020. The analysis includes a time series analysis to track the distribution of data and content analysis to analyze the knowledge and attitudes of Nigerians. A total of 67,989 tweets (1,484 unique and 66,505 retweets) citing COVID-19 and related keywords were returned. The Tweets started to emerge earlier to the first confirmed case in Nigeria while maintaining a dangling-upward movement up to the 11th week under study.

Matters arising from the tweets include a dearth of information on COVID-19 and optimism among others. The results provide insight into the intersection of SNSs and public health surveillance. Results show how helpful Twitter is to educate education in public health. Health organizations and the government may benefit from paying attention to both amusing and emotional contents from the Twitter community to formulate a viable policy for treatment and control.

Reference

https://www.cell.com/heliyon/fulltext/S2405-8440(21)01287-1

Publication Date: May 29, 2021

COVID-19: Rapid antigen detection for SARS-CoV-2 by lateral flow assay: A national systematic evaluation of sensitivity and specificity for mass-testing

Abstract

Background: Lateral flow device (LFD) viral antigen immunoassays have been developed around the world as diagnostic tests for SARS-CoV-2 infection. They have been proposed to deliver an infrastructure-light, cost-economical solution giving results within half an hour.

Methods: LFDs were initially reviewed by a Department of Health and Social Care team, part of the UK government, from which 64 were selected for further evaluation from 1st August to 15th December 2020. Standardised laboratory evaluations, and for those that met the published criteria, field testing in the Falcon-C19 research study and UK pilots were performed (UK COVID-19 testing centres, hospital, schools, armed forces).

Findings: 4/64 LFDs so far have desirable performance characteristics (orient Gene, Deepblue, Abbott and Innova SARS-CoV-2 Antigen Rapid Qualitative Test). All these LFDs have a viral antigen detection of >90% at 100,000 RNA copies/ml. 8951 Innova LFD tests were performed with a kit failure rate of 5.6% (502/8951, 95% CI: 5.1–6.1), false positive rate of 0.32% (22/6954, 95% CI: 0.20–0.48). Viral antigen detection/sensitivity across the sampling cohort when performed by laboratory scientists was 78.8% (156/198, 95% CI 72.4–84.3).

Interpretation: The results suggest LFDs have promising performance characteristics for mass population testing and can be used to identify infectious positive individuals. The Innova LFD shows good viral antigen detection/sensitivity with excellent specificity, although kit failure rates and the impact of training are potential issues. These results support the expanded evaluation of LFDs, and assessment of greater access to testing on COVID-19 transmission.

Reference

https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00204-2/fulltext

Publication Date: May 28, 2021

Interrelationship between daily COVID-19 cases and average temperature as well as relative humidity in Germany

Abstract

COVID-19 pandemic continues to obstruct social lives and the world economy other than questioning the healthcare capacity of many countries. Weather components recently came to notice as the northern hemisphere was hit by escalated incidence in winter. This study investigated the association between COVID-19 cases and two components, average temperature and relative humidity, in the 16 states of Germany. Three main approaches were carried out in this study, namely temporal correlation, spatial auto-correlation, and clustering-integrated panel regression. It is claimed that the daily COVID-19 cases correlate negatively with the average temperature and positively with the average relative humidity. To extract the spatial auto-correlation, both global Moran's {\mathscr {I}} and global Geary's {\mathscr {C}} were used whereby no significant difference in the results was observed. It is evident that randomness overwhelms the spatial pattern in all the states for most of the observations, except in recent observations where either local clusters or dispersion occurred. This is further supported by Moran's scatter plot, where states' dynamics to and fro cold and hot spots are identified, rendering a traveling-related early warning system. A random-effects model was used in the sense of case-weather regression including incidence clustering. Our task is to perceive which ranges of the incidence that are well predicted by the existing weather components rather than seeing which ranges of the weather

components predicting the incidence. The proposed clustering-integrated model associated with optimal barriers articulates the data well whereby weather components outperform lag incidence cases in the prediction. Practical implications based on marginal effects follow posterior to model diagnostics.

Reference

https://www.nature.com/articles/s41598-021-90873-5

Laboratory trends, hyperinflammation, and clinical outcomes for patients with a systemic rheumatic disease admitted to hospital for COVID-19: A retrospective, comparative cohort study

Abstract

Background: COVID-19 can induce a hyperinflammatory state, which might lead to poor clinical outcomes. It was aimed to assess whether patients with a systemic rheumatic disease might be at increased risk for hyperinflammation and respiratory failure from COVID-19.

Methods: A retrospective, comparative cohort study of patients aged 18 years or older was done, which were admitted to hospital with PCR-confirmed COVID-19 at Mass General Brigham (Boston, USA). We identified patients by a search of electronic health records and matched patients with a systemic rheumatic disease 1:5 to comparators. Individual laboratory results were compared by case status and extracted laboratory results and COVID-19 outcomes for each participant. The COVID-19-associated hyperinflammation score (cHIS) was calculated, a composite of six domains (a score of ≥2 indicating hyperinflammation) and used logistic regression to estimate odds ratios (ORs) for COVID-19 outcomes by hyperinflammation and case status.

Findings: 57 Patients were identified with a systemic rheumatic disease and 232 matched comparators who were admitted to hospital with COVID-19 between Jan 30 and July 7, 2020; 38 (67%) patients with a rheumatic disease were female compared with 158 (68%) matched comparators. Patients with a systemic rheumatic disease had higher peak median neutrophil-to-lymphocyte ratio (9·6 [IQR 6·4–22·2] vs 7·8 [4·5–16·5]; p=0·021), lactate dehydrogenase concentration (421 U/L [297–528] vs 345 U/L [254–479]; p=0·044), creatinine concentration (1·2 mg/dL [0·9–2·0] vs 1·0 mg/dL [0·8–

1·4], p=0·014), and blood urea nitrogen concentration (31 mg/dL [15–61] vs 23 mg/dL [13–37]; p=0·033) than comparators, but median C-reactive protein concentration (149·4 mg/L [76·4–275·3] vs 116·3 mg/L [58·8–225·9]; p=0·11) was not significantly different. Patients with a systemic rheumatic disease had higher peak median cHIS than comparators (3 [1–5] vs 2 [1–4]; p=0·013). All patients with a peak cHIS of 2 or more had higher odds of admission to intensive care (OR 3·45 [95% CI 1·98–5·99]), mechanical ventilation (66·20 [8·98–487·80]), and in-hospital mortality (16·37 [4·75–56·38]) than patients with a peak cHIS of less than 2. In adjusted analyses, patients with a rheumatic disease had higher odds of admission to intensive care (2·08 [1·09–3·96]) and mechanical ventilation (2·60 [1·32–5·12]) than comparators, but not in-hospital mortality (1.78 [0·79–4·02]). Among patients who were discharged from hospital, risk of rehospitalisation (1·08 [0·37–3·16]) and mortality within 60 days (1·20 [0·58–2·47]) was similar in patients and comparators.

Interpretation: Patients with a systemic rheumatic disease who were admitted to hospital for COVID-19 had increased risk for hyperinflammation, kidney injury, admission to intensive care, and mechanical ventilation compared with matched comparators. However, among patients who survived, post-discharge outcomes were not significantly different. The cHIS identified patients with hyperinflammation, which was strongly associated with poor COVID-19 outcomes in both patients with a rheumatic disease and comparators. Clinicians should be aware that patients with systemic rheumatic diseases and COVID-19 could be susceptible to hyperinflammation and poor hospital outcomes.

Reference

https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(21)00140-5/fulltext

Publication Date: May 27, 2021

BNT162b2 vaccine induces neutralizing antibodies and poly-specific T cells in humans

Absract

BNT162b2, a nucleoside-modified mRNA formulated in lipid nanoparticles that encodes the SARS-CoV-2 spike glycoprotein (S) stabilized in its prefusion conformation, has

demonstrated 95% efficacy in preventing COVID-191. Here we extend a previous phase-I/II trial report2 by presenting data on the immune response induced by BNT162b2 prime–boost vaccination from an additional phase-I/II trial in healthy adults (18–55 years old). BNT162b2 elicited strong antibody responses: at one week after the boost, SARS-CoV-2 serum geometric mean 50% neutralizing titres were up to 3.3-fold above those observed in samples from individuals who had recovered from COVID-19. Sera elicited by BNT162b2 neutralized 22 pseudoviruses bearing the S of different SARS-CoV-2 variants. Most participants had a strong response of IFNγ+ or IL-2+ CD8+ and CD4+ T helper type 1 cells, which was detectable throughout the full observation period of nine weeks following the boost. Using peptide–MHC multimer technology, we identified several BNT162b2-induced epitopes that were presented by frequent MHC alleles and conserved in mutant strains. One week after the boost, epitope-specific CD8+ T cells of the early-differentiated effector-memory phenotype comprised 0.02–2.92% of total circulating CD8+ T cells and were detectable (0.01–0.28%) eight weeks later. In summary, BNT162b2 elicits an adaptive humoral and poly-specific cellular immune response against epitopes that are conserved in a broad range of variants, at well-tolerated doses.

Reference

https://www.nature.com/articles/s41586-021-03653-6

Effects of potent neutralizing antibodies from convalescent plasma in patients hospitalized for severe SARS-CoV-2 infection

Absract

In a randomized clinical trial of 86 hospitalized COVID-19 patients comparing standard care to treatment with 300mL convalescent plasma containing high titers of neutralizing SARS-CoV-2 antibodies, no overall clinical benefit was observed. Using a comprehensive translational approach, we unravel the virological and immunological responses following treatment to disentangle which COVID-19 patients may benefit and should be the focus of future studies. Convalescent plasma is safe, does not improve survival, has no effect on the disease course, nor does plasma enhance viral clearance in the respiratory tract, influence SARS-CoV-2 antibody development or serum proinflammatory cytokines levels. Here, we show that the vast majority of patients

already had potent neutralizing SARS-CoV-2 antibodies at hospital admission and with comparable titers to carefully selected plasma donors. This resulted in the decision to terminate the trial prematurely. Treatment with convalescent plasma should be studied early in the disease course or at least preceding autologous humoral response development.

Reference

https://www.nature.com/articles/s41467-021-23469-2

Dynamic changes in gene-to-gene regulatory networks in response to SARS-CoV-2 infection

Absract

The current pandemic of SARS-CoV-2 has caused extensive damage to society. The characterization of SARS-CoV-2 profiles has been addressed by researchers globally with the aim of resolving this disruptive crisis. This investigation process is indispensable to understand how SARS-CoV-2 behaves in human host cells. However, little is known about the systematic molecular mechanisms involved in the effects of SARS-CoV-2 infection on human host cells. Here, gene-to-gene regulatory networks were presented in response to SARS-CoV-2 using a Bayesian network. The dynamic changes were examined in the SARS-CoV-2-purturbated networks established by our proposed framework for gene network analysis, thus revealing that interferon signaling gradually switched to the subsequent inflammatory cytokine signaling cascades. Furthermore, we succeeded in capturing a COVID-19 patient-specific network in which transduction of these signals was concurrently induced. This enabled us to explore the local regulatory systems influenced by SARS-CoV-2 in host cells more precisely at an individual level. The panel of network analyses has provided new insights into SARS-CoV-2 research from the perspective of cellular systems.

Reference

https://www.nature.com/articles/s41598-021-90556-1

Viral fibrotic scoring and drug screen based on MAPK activity uncovers EGFR as a key regulator of COVID-19 fibrosis

Absract

Understanding the molecular basis of fibrosis, the lethal complication of COVID-19, is urgent. By the analysis of RNA-sequencing data of SARS-CoV-2-infected cells combined with data mining we identified genes involved in COVID-19 progression. To characterize their implication in the fibrosis development we established a correlation matrix based on the transcriptomic data of patients with idiopathic pulmonary fibrosis. With this method, we have identified a cluster of genes responsible for SARS-CoV-2-fibrosis including its entry receptor ACE2 and epidermal growth factor EGF. Then, Vi-Fi scoring was developed, which was a novel drug repurposing approach and simultaneously quantified antiviral and antifibrotic activities of the drugs based on their transcriptomic signatures. It was revealed the strong dual antifibrotic and antiviral activity of EGFR/ErbB inhibitors. Before the in vitro validation, we have clustered 277 cell lines and revealed distinct COVID-19 transcriptomic signatures of the cells with similar phenotypes that defines their suitability for COVID-19 research. By ERK activity monitoring in living lung cells, we show that the drugs with predicted antifibrotic activity downregulate ERK in the host lung cells. Overall, the study provides novel insights on SARS-CoV-2 dependence on EGFR/ERK signaling and demonstrates the utility of EGFR/ErbB inhibitors for COVID-19 treatment.

Reference

https://www.nature.com/articles/s41598-021-90701-w

Toward understanding COVID-19 pneumonia: A deep-learning-based approach for severity analysis and monitoring the disease

Absract

A new approach was reported using artificial intelligence (AI) to study and classify the severity of COVID-19 using 1208 chest X-rays (CXRs) of 396 COVID-19 patients obtained through the course of the disease at Emory Healthcare affiliated hospitals (Atlanta, GA, USA). Using a two-stage transfer learning technique to train a convolutional neural network (CNN), we show that the algorithm is able to classify four

classes of disease severity (normal, mild, moderate, and severe) with the average Area Under the Curve (AUC) of 0.93. In addition, we show that the outputs of different layers of the CNN under dominant filters provide valuable insight about the subtle patterns in the CXRs, which can improve the accuracy in the reading of CXRs by a radiologist. Finally, we show that our approach can be used for studying the disease progression in a single patient and its influencing factors. The results suggest that the technique can form the foundation of a more concrete clinical model to predict the evolution of COVID-19 severity and the efficacy of different treatments for each patient through using CXRs and clinical data in the early stages of the disease. This use of AI to assess the severity and possibly predicting the future stages of the disease early on, will be essential in dealing with the upcoming waves of COVID-19 and optimizing resource allocation and treatment.

Reference

https://www.nature.com/articles/s41598-021-90411-3

Androgen regulation of pulmonary AR, TMPRSS2 and ACE2 with implications for sex-discordant COVID-19 outcomes

Absract

The sex discordance in COVID-19 outcomes has been widely recognized, with males generally faring worse than females and a potential link to sex steroids. A plausible mechanism is androgen-induced expression of TMPRSS2 and/or ACE2 in pulmonary tissues that may increase susceptibility or severity in males. This hypothesis is the subject of several clinical trials of anti-androgen therapies around the world. Here, the sex-associated TMPRSS2 and ACE2 expressions in human and mouse lungs were investigated and interrogated the possibility of pharmacologic modification of their expression with anti-androgens. No evidence was found for increased TMPRSS2 expression in the lungs of males compared to females in humans or mice. Furthermore, in male mice, treatment with the androgen receptor antagonist enzalutamide did not decrease pulmonary TMPRSS2. On the other hand, ACE2 and AR expression was sexually dimorphic and higher in males than females. ACE2 was moderately suppressible with enzalutamide administration. The work suggests that sex differences

in COVID-19 outcomes attributable to viral entry are independent of TMPRSS2. Modest changes in ACE2 could account for some of the sex discordance.

Reference

https://www.nature.com/articles/s41598-021-90491-1

SARS-CoV-2 infection paralyzes cytotoxic and metabolic functions of the immune cells

Absract

The SARS-CoV-2 virus is the causative agent of the global COVID-19 infectious disease outbreak, which can lead to acute respiratory distress syndrome (ARDS). However, it is still unclear how the virus interferes with immune cell and metabolic functions in the human body. In this study, we investigated the immune response in acute or convalescent COVID-19 patients. It was characterized that the peripheral blood mononuclear cells (PBMCs) using flow cytometry and found that CD8+ T cells were significantly subsided in moderate COVID-19 and convalescent patients. Furthermore, characterization of CD8+ T cells suggested that convalescent patients have significantly diminished expression of both perforin and granzyme A. Using ^{1}H-NMR spectroscopy, we characterized the metabolic status of their autologous PBMCs. It was found that fructose, lactate and taurine levels were elevated in infected (mild and moderate) patients compared with control and convalescent patients. Glucose, glutamate, formate and acetate levels were attenuated in COVID-19 (mild and moderate) patients. In summary, the report suggests that SARS-CoV-2 infection leads to disrupted CD8+ T cytotoxic functions and changes the overall metabolic functions of immune cells.

Reference

https://www.cell.com/heliyon/fulltext/S2405-8440(21)01250-0

Same-day SARS-CoV-2 antigen test screening in an indoor mass-gathering live music event: A randomised controlled trial

Absract

Background: The banning of mass-gathering indoor events to prevent SARS-CoV-2 spread has had an important effect on local economies. Despite growing evidence on

the suitability of antigen-detecting rapid diagnostic tests (Ag-RDT) for mass screening at the event entry, this strategy has not been assessed under controlled conditions. It was aimed to assess the effectiveness of a prevention strategy during a live indoor concert.

Methods: A randomised controlled open-label trial was designed to assess the effectiveness of a comprehensive preventive intervention for a mass-gathering indoor event (a live concert) based on systematic same-day screening of attendees with Ag-RDTs, use of facial masks, and adequate air ventilation. The event took place in the Sala Apolo, Barcelona, Spain. Adults aged 18–59 years with a negative result in an Ag-RDT from a nasopharyngeal swab collected immediately before entering the event were randomised 1:1 (block randomisation stratified by age and gender) to either attend the indoor event for 5 hours or go home. Nasopharyngeal specimens used for Ag-RDT screening were analysed by real-time reverse-transcriptase PCR (RT-PCR) and cell culture (Vero E6 cells). 8 days after the event, a nasopharyngeal swab was collected and analysed by Ag-RDT, RT-PCR, and a transcription-mediated amplification test (TMA). The primary outcome was the difference in incidence of RT-PCR-confirmed SARS-CoV-2 infection at 8 days between the control and the intervention groups, assessed in all participants who were randomly assigned, attended the event, and had a valid result for the SARS-CoV-2 test done at follow-up. The trial is registered at ClinicalTrials.gov, NCT04668625.

Findings: Participant enrollment took place during the morning of the day of the concert, Dec 12, 2020. Of the 1140 people who responded to the call and were deemed eligible, 1047 were randomly assigned to either enter the music event (experimental group) or continue with normal life (control group). Of the 523 randomly assigned to the experimental group, 465 were included in the analysis of the primary outcome (51 did not enter the event and eight did not take part in the follow-up assessment), and of the 524 randomly assigned to the control group, 495 were included in the final analysis (29 did not take part in the follow-up). At baseline, 15 (3%) of 495 individuals in the control group and 13 (3%) of 465 in the experimental group tested positive on TMA despite a negative Ag-RDT result. The RT-PCR test was positive in one case in each group and cell viral culture was negative in all cases. 8 days after the event, two (<1%) individuals in the control arm had a positive Ag-RDT and PCR result, whereas no Ag-RDT nor RT-PCR positive results were found in the intervention arm. The Bayesian estimate for the

incidence between the experimental and control groups was –0·15% (95% CI –0·72 to 0·44).

Interpretation: The study provides preliminary evidence on the safety of indoor mass-gathering events during a COVID-19 outbreak under a comprehensive preventive intervention. The data could help restart cultural activities halted during COVID-19, which might have important sociocultural and economic implications.

Reference

https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00268-1/fulltext

Colchicine for community-treated patients with COVID-19 (COLCORONA): A phase 3, randomised, double-blinded, adaptive, placebo-controlled, multicentre trial

Abstract

Background: Evidence suggests a role for excessive inflammation in COVID-19 complications. Colchicine is an oral anti-inflammatory medication beneficial in gout, pericarditis, and coronary disease. It was aimed to investigate the effect of colchicine on the composite of COVID-19-related death or hospital admission.

Methods: The present study is a phase 3, randomised, double-blind, adaptive, placebo-controlled, multicentre trial. The study was done in Brazil, Canada, Greece, South Africa, Spain, and the USA, and was led by the Montreal Heart Institute. Patients with COVID-19 diagnosed by PCR testing or clinical criteria who were not being treated in hospital were eligible if they were at least 40 years old and had at least one high-risk characteristic. The randomisation list was computer-generated by an unmasked biostatistician, and masked randomisation was centralised and done electronically through an automated interactive web-response system. The allocation sequence was unstratified and used a 1:1 ratio with a blocking schema and block sizes of six. Patients were randomly assigned to receive orally administered colchicine (0·5 mg twice per day for 3 days and then once per day for 27 days thereafter) or matching placebo. The primary efficacy endpoint was the composite of death or hospital admission for COVID-19. Vital status at the end of the study was available for 97·9% of patients. The analyses were done according to the intention-to-treat principle. The COLCORONA trial

is registered with ClinicalTrials.gov (NCT04322682) and is now closed to new participants.

Findings: Trial enrolment began in March 23, 2020, and was completed in Dec 22, 2020. A total of 4488 patients (53·9% women; median age 54·0 years, IQR 47·0–61·0) were enrolled and 2235 patients were randomly assigned to colchicine and 2253 to placebo. The primary endpoint occurred in 104 (4·7%) of 2235 patients in the colchicine group and 131 (5·8%) of 2253 patients in the placebo group (odds ratio [OR] 0·79, 95·1% CI 0·61–1·03; p=0·081). Among the 4159 patients with PCR-confirmed COVID-19, the primary endpoint occurred in 96 (4·6%) of 2075 patients in the colchicine group and 126 (6·0%) of 2084 patients in the placebo group (OR 0·75, 0·57–0·99; p=0·042). Serious adverse events were reported in 108 (4·9%) of 2195 patients in the colchicine group and 139 (6·3%) of 2217 patients in the placebo group (p=0·051); pneumonia occurred in 63 (2·9%) of 2195 patients in the colchicine group and 92 (4·1%) of 2217 patients in the placebo group (p=0·021). Diarrhoea was reported in 300 (13·7%) of 2195 patients in the colchicine group and 161 (7·3%) of 2217 patients in the placebo group (p<0·0001).

Interpretation: In community-treated patients including those without a mandatory diagnostic test, the effect of colchicine on COVID-19-related clinical events was not statistically significant. Among patients with PCR-confirmed COVID-19, colchicine led to a lower rate of the composite of death or hospital admission than placebo. Given the absence of orally administered therapies to prevent COVID-19 complications in community-treated patients and the benefit of colchicine in patients with PCR-proven COVID-19, this safe and inexpensive anti-inflammatory agent could be considered for use in those at risk of complications. Notwithstanding these considerations, replication in other studies of PCR-positive community-treated patients is recommended.

Reference

https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00222-8/fulltext

Evaluation of SARS-CoV-2 IgG antibody reactivity in patients with systemic lupus erythematosus: Analysis of a multi-racial and multi-ethnic cohort

Abstract

Background: Patients with systemic lupus erythematosus (SLE) are at risk of developing COVID-19 due to underlying immune abnormalities and regular use of immunosuppressant medications. It was aimed to evaluate the presence of SARS-CoV-2 IgG antibodies in patients with SLE with or without previous COVID-19-related symptoms or RT-PCR-confirmed SARS-CoV-2 infection.

Methods: For this analysis, patients with SLE were included from two cohorts based in New York City: the Web-based Assessment of Autoimmune, Immune-Mediated and Rheumatic Patients during the COVID-19 pandemic (WARCOV) study; and the NYU Lupus Cohort (a prospective registry of patients at NYU Langone Health and NYC Health + Hospitals/Bellevue). Patients in both cohorts were tested for SARS-CoV-2 IgG antibodies via commercially available immunoassays, processed through hospital or outpatient laboratories. Patients recruited from the NYU Lupus Cohort, referred from affiliated providers, or admitted to hospital with COVID-19 were tested for SARS-CoV-2 IgG antibodies as part of routine surveillance during follow-up clinical visits.

Findings: 329 Patients with SLE were included in this analysis, 146 from the WARCOV study and 183 from the NYU Lupus Cohort, and were tested for SARS-CoV-2 antibodies between April 29, 2020, and Feb 9, 2021. 309 (94%) were women and 91 (28%) were of Hispanic ethnicity. 51 (16%) of 329 patients had a positive SARS-CoV-2 IgG antibody test. Seropositive patients were more likely than seronegative patients to be Hispanic (24 [47%] of 51 vsz 67 [24%] of 278). Other demographic variables, SLE-specific factors, and immunosuppressant use were not associated with SARS-CoV-2 positivity. Of the 29 patients with COVID-19 previously confirmed by RT-PCR, 18 (62%) were on immunosuppressants; 24 (83%) of 29 patients tested positive for SARS-CoV-2 IgG antibodies. Of 17 patients who had symptoms of COVID-19 but negative concurrent RT-PCR testing, one (6%) developed an antibody response. Of 26 patients who had COVID-19-related symptoms but did not undergo RT-PCR testing, six (23%) developed an antibody response. Of 83 patients who had no symptoms of COVID-19 and no RT-PCR testing, four (5%) developed an antibody response. Among 36 patients who were

initially SARS-CoV-2 IgG positive, the majority maintained reactivity serially (88% up to 10 weeks, 83% up to 20 weeks, and 80% up to 30 weeks). Seven (70%) of ten patients with confirmed COVID-19 had antibody positivity beyond 30 weeks from disease onset.

Interpretation: Most patients with SLE and confirmed COVID-19 were able to produce and maintain a serological response despite the use of a variety of immunosuppressants, providing reassurance about the efficacy and durability of humoral immunity and possible protection against re-infection with SARS-CoV-2.

Reference

https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(21)00114-4/fulltext

Systemic lupus erythematosus does not prevent antibody responses to SARS-CoV-2

Abstract

From the beginning of the COVID-19 pandemic, patients with systemic lupus erythematosus (SLE) were particularly concerned about their risks following exposure to the virus and so were the physicians caring for them. After all, it seemed entirely possible that SLE and its therapy might reduce the immune response to SARS-CoV-2 and increase the risk of severe COVID-19 outcomes. Owing to immunoglobulin and immune complex formation and the ensuing release of interferons, SLE mimics much of the immune response against viral infection. Accordingly, therapeutic action in SLE is designed to disrupt these feedback loops and to reduce the formation of antibodies. In March–April, 2020, patients with SLE were more commonly admitted to hospital for COVID-19 than the general population, and in a study done between April 13 and June 1, 2020, in New York City, four of 41 patients with SLE and RT-PCR-confirmed SARS-CoV-2 infection died, although it should be noted that three of these four patients refused intubation.

As more data became available, most of the fears surrounding COVID-19 outcomes in patients with SLE were alleviated. The proportion of hospital admissions for patients with SLE diagnosed with COVID-19 was not significantly increased compared to patients with other rheumatic diseases (odds ratio [OR] 1·80; 95% CI 0·99–3·29; p=0·06), which might be explained in part by increased caution. Compared to patients

with rheumatoid arthritis, a diagnosis of SLE was not associated with an increased odds of death from COVID-19 (OR 1·2; 95% CI 0·70–2·04), despite a higher prevalence of organ damage in this group.

Reference

https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(21)00153-3/fulltext

Same-day SARS-CoV-2 antigen test screening in an indoor mass-gathering live music event: A randomised controlled trial

Abstract

Background: The banning of mass-gathering indoor events to prevent SARS-CoV-2 spread has had an important effect on local economies. Despite growing evidence on the suitability of antigen-detecting rapid diagnostic tests (Ag-RDT) for mass screening at the event entry, this strategy has not been assessed under controlled conditions. We aimed to assess the effectiveness of a prevention strategy during a live indoor concert.

Methods: A randomised controlled open-label trial was designed to assess the effectiveness of a comprehensive preventive intervention for a mass-gathering indoor event (a live concert) based on systematic same-day screening of attendees with Ag-RDTs, use of facial masks, and adequate air ventilation. The event took place in the Sala Apolo, Barcelona, Spain. Adults aged 18–59 years with a negative result in an Ag-RDT from a nasopharyngeal swab collected immediately before entering the event were randomised 1:1 (block randomisation stratified by age and gender) to either attend the indoor event for 5 hours or go home. Nasopharyngeal specimens used for Ag-RDT screening were analysed by real-time reverse-transcriptase PCR (RT-PCR) and cell culture (Vero E6 cells). 8 Days after the event, a nasopharyngeal swab was collected and analysed by Ag-RDT, RT-PCR, and a transcription-mediated amplification test (TMA). The primary outcome was the difference in incidence of RT-PCR-confirmed SARS-CoV-2 infection at 8 days between the control and the intervention groups, assessed in all participants who were randomly assigned, attended the event, and had a valid result for the SARS-CoV-2 test done at follow-up. The trial is registered at ClinicalTrials.gov, NCT04668625.

Findings: Participant enrollment took place during the morning of the day of the concert, Dec 12, 2020. Of the 1140 people who responded to the call and were deemed eligible, 1047 were randomly assigned to either enter the music event (experimental group) or continue with normal life (control group). Of the 523 randomly assigned to the experimental group, 465 were included in the analysis of the primary outcome (51 did not enter the event and eight did not take part in the follow-up assessment), and of the 524 randomly assigned to the control group, 495 were included in the final analysis (29 did not take part in the follow-up). At baseline, 15 (3%) of 495 individuals in the control group and 13 (3%) of 465 in the experimental group tested positive on TMA despite a negative Ag-RDT result. The RT-PCR test was positive in one case in each group and cell viral culture was negative in all cases. 8 days after the event, two (<1%) individuals in the control arm had a positive Ag-RDT and PCR result, whereas no Ag-RDT nor RT-PCR positive results were found in the intervention arm. The Bayesian estimate for the incidence between the experimental and control groups was –0·15% (95% CI –0·72 to 0·44).

Interpretation: The study provides preliminary evidence on the safety of indoor mass-gathering events during a COVID-19 outbreak under a comprehensive preventive intervention. The data could help restart cultural activities halted during COVID-19, which might have important sociocultural and economic implications.

Reference

https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00268-1/fulltext

CORRESPONDANCE

Publication Date: Jun 02, 2021

Gene therapy avenues and COVID-19 vaccines

2020 has witnessed unprecedented situations due to coronavirus pandemic that affected all aspects of life. The whole globe lived months of uncertainty before two companies have announced the incredible results of phase III clinical trials for two different mRNA-based vaccines. For more details, read the link given below.

Reference

https://www.nature.com/articles/s41435-021-00136-6

Publication Date: May 27, 2021

Serum neutralising activity against SARS-CoV-2 variants elicited by CoronaVac

Emergence of multiple SARS-CoV-2 variants of concern (VOCs) harbouring mutations in the spike protein—the major target of neutralising antibodies—has raised serious concerns about the potential for reduced protective efficacy of humoral responses elicited by vaccination. CoronaVac (Sinovac Biotech, Beijing, China) is an inactivated vaccine that has been authorised for conditional mass use against COVID-19 in China and was efficacious in preventing symptomatic and severe disease in a phase 3 trial.

To evaluate the potential resistance of new variants to neutralisation elicited by CoronaVac, sera from 93 healthy health-care professionals from Nanjing Drum Tower Hospital, a tertiary hospital in Nanjing, China, who received two doses of CoronaVac were obtained before the first dose and at day 14 after two doses. We assayed their neutralisation activity against lentivirus-based SARS-CoV-2 pseudotyped viruses containing the spike protein of the Wuhan-1 reference strain (wildtype), as well as six circulating variants, including D614G, B.1.1.7 (first identified in the UK), B.1.351 (first identified in South Africa), P.1 (first identified in Brazil), B.1.429 (first identified in California, USA), and B.1.526 (first identified in New York, NY, USA).

Reference

https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00287-5/fulltext

COMMENT

Publication Date: Jun 02, 2021

The emerging osteo-metabolic phenotype of COVID-19: clinical and pathophysiological aspects

An emerging feature of COVID-19 is a clinically relevant osteo-metabolic phenotype characterized by widespread acute hypocalcaemia and chronic hypovitaminosis D with high prevalence of vertebral fractures. This phenotype might have negative effects on disease severity and its components could represent possible targets for prevention of SARS-CoV-2 infection and poor COVID-19 outcomes. For more details, read the given link below.

Reference

https://www.nature.com/articles/s41574-021-00516-y

Publication Date: May 28, 2021

Negative antigen RDT and RT-PCR results do not rule out COVID-19 if clinical suspicion is strong

Yap Boum and colleagues brought significant insight into the importance of rapid diagnostic tests for SARS-CoV-2. Boum and colleagues provided useful information about the patterns of patient presentation. However, some important considerations lead us to suggest an improvement to the algorithm they describe in figure 2A. The feeling is that the clinical context for the suspicion of COVID-19 warrants consideration. Indeed, it is not unusual to see patients with a suggestive clinical presentation, with or without chest CT imaging features suggestive of COVID-19, but negative rapid diagnostic or RT-PCR test results. These false-negative results could be explained by a number of factors: viral load, which is associated with disease course and disease severity; sputum or throat swab sample quality, which must contain sufficient cellular material for detection; kit performance; sample transportation and sample storage conditions; lack of standardised operating procedures; interpretation of results; and quality-control issues. Moreover, patients with high platelet counts or C-reactive protein

levels are at increased risk of having false-negative first RT-PCR results. Finally, in the presence of a negative screening result for SARS-CoV-2, clinicians should not ignore potential differential diagnoses, which should be ruled out. As shown in the appendix, we propose in case of strong clinical suspicion but negative antigen rapid diagnostic tests or RT-PCR results that the patient is re-sampled by a different operator from the one who did the first test. Furthermore, adding antibody-based tests to the proposed armamentarium of diagnostic tools for COVID-19 in symptomatic individuals could improve the positive predictive value of the whole strategy. Also, in patients with a high clinical suspicion, performing up to three tests, as suggested by some authors, would be wise before ruling out the diagnosis. Nevertheless, if clinical suspicion remains strong, chest CT imaging should be done, even in resource-limited settings, because of its reasonably good sensitivity and severity-grading role. For more details, read the given link below.

Reference

https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00271-1/fulltext

Defining COVID-19-associated hyperinflammatory syndrome in specific populations

Among the unique characteristics of COVID-19 is a predilection to elicit a maladaptive immune response leading to excessive inflammation and organ injury. This complication of severe COVID-19 is associated with poor outcomes, shares characteristics with other cytokine storm or hyperinflammatory syndromes, and is the target for a variety of immunomodulatory therapeutics. Defining this syndrome and identifying which patient populations are at highest risk of developing hyperinflammation are high clinical priorities. Identifying this risk is particularly important in patients with underlying systemic rheumatic diseases for several reasons. First, patients with these diseases often have an elevated inflammatory setpoint and might be more likely to develop secondary hyperinflammatory syndromes. Second, immunomodulatory therapies used in patients with systemic rheumatic diseases might variably affect susceptibility to COVID-19 and its associated hyperinflammatory syndrome. For example, some therapies, such as tumour necrosis factor inhibitors, have been posited to temper complications associated with COVID-19 hyperinflammation. Alternatively, drugs that

impair humoral immunity, such as anti-CD19 monoclonal antibodies or non-selective antiproliferative drugs, might prolong the active virological phase of COVID-19, leading to perpetuated lung injury, persistent or relapsing inflammation, and poor outcomes. Finally, the interaction between systemic inflammation and immunomodulatory therapy and COVID-19 prognosis is further complicated by the high prevalence of chronic diseases in patients with systemic rheumatic diseases that independently increase risk for poor outcomes in COVID-19. For more details, read the given link below.

Reference

https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(21)00157-0/fulltext

REPORT

Publication Date: May 27, 2021

Broad auto-reactive IgM responses are common in critically ill patients, including those with COVID-19

The pathogenesis of severe coronavirus disease 2019 (COVID-19) remains poorly understood. While several studies suggest that immune dysregulation plays a central role, the key mediators of this process are yet to be defined. Here, we demonstrate that plasma from a high proportion (93%) of critically ill COVID-19 patients, but not healthy controls, contains broadly auto-reactive immunoglobulin M (IgM) and less frequently auto-reactive IgG or IgA. Importantly, these auto-IgMs preferentially recognize primary human lung cells in vitro, including pulmonary endothelial and epithelial cells. By using a combination of flow cytometry, analytical proteome microarray technology, and lactose dehydrogenase (LDH)-release cytotoxicity assays, we identify high-affinity, complement-fixing, auto-reactive IgM directed against 260 candidate autoantigens, including numerous molecules preferentially expressed on the cellular membranes of pulmonary, vascular, gastrointestinal, and renal tissues. These findings suggest that broad IgM-mediated autoimmune reactivity may be involved in the pathogenesis of severe COVID-19, thereby identifying a potential target for therapeutic interventions.

Reference

https://www.cell.com/cell-reports-medicine/fulltext/S2666-3791(21)00164-6