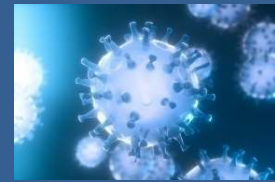


COVID-19

May 20 - 26, 2021



RESEARCH PUBLICATIONS

Publication Date: May 26, 2021

Influenza vaccination and the risk of COVID-19 infection and severe illness in older adults in the United States

Abstract

The coronavirus disease of 2019 (COVID-19) has caused a global pandemic and led to nearly three million deaths globally. As of April 2021, there are still many countries that do not have COVID-19 vaccines. Before the COVID-19 vaccines were developed, some evidence suggested that an influenza vaccine may stimulate nonspecific immune responses that reduce the risk of COVID-19 infection or the severity of COVID-19 illness after infection. This study evaluated the association between influenza vaccination and the risk of COVID-19 infection. A retrospective cross-sectional study was conducted with data from July 1, 2019, to June 30, 2020 with the Claims data from Symphony Health database. The study population was adults age 65 years old or older who received influenza vaccination between September 1 and December 31 of 2019. The main outcomes and measures were odds of COVID-19 infection and severe COVID-19 illness after January 15, 2020. The adjusted odds ratio (aOR) of COVID-19 infection risk was found between the influenza-vaccination group and no-influenza-vaccination group was 0.76 (95% confidence interval (CI), 0.75–0.77). Among COVID-19 patients, the aOR of developing severe COVID-19 illness was 0.72 (95% CI, 0.68–0.76) between the influenza-vaccination group and the no-influenza-vaccination group. When the influenza-vaccination group and the other-vaccination group were compared, the aOR of COVID-19 infection was 0.95 (95% CI, 0.93–0.97), and the aOR of developing a severe COVID-19 illness was 0.95 (95% CI, 0.80–1.13). The influenza vaccine may marginally protect people from COVID-19 infection.

Reference

<https://www.nature.com/articles/s41598-021-90068-y>

Ocular findings among patients surviving COVID-19

Abstract

To describe the medium-term ophthalmological findings in patients recovering from COVID-19. Patients recovered from the acute phase of COVID-19 underwent a complete ophthalmological evaluation, including presenting and best-corrected visual acuity (BCVA), refractometry, biomicroscopy, tonometry, break-up time and Schirmer tests, indirect ophthalmoscopy, color fundus picture, and retinal architecture evaluation using optical coherence tomography. Socio-demographic data and personal medical history were also collected. According to the severity of systemic manifestations, patients were classified into mild-to-moderate, severe, and critical. Sixty-four patients (128 eyes) were evaluated 82 ± 36.4 days after the onset of COVID's symptoms. The mean \pm SD duration of hospitalization was 15.0 ± 10.7 days. Seven patients (10.9%) had mild-to-moderate, 33 (51.5%) severe, and 24 (37.5%) critical disease. Median [interquartile ranges (IQR)] presenting visual acuity was 0.1 (0–0.2) and BCVA 0 (0–0.1). Anterior segment biomicroscopy was unremarkable, except for dry eye disease, verified in 10.9% of them. The mean \pm SD intraocular pressure (IOP) in critical group (14.16 ± 1.88 mmHg) was significantly higher than in severe group (12.51 ± 2.40 mmHg), both in the right (p 0.02) and left eyes (p 0.038). Among all, 15.6% had diabetic retinopathy, and two patients presented with discrete white-yellowish dots in the posterior pole, leading to hyporreflective changes at retinal pigment epithelium level, outer segment, and ellipsoid layers. The present study identified higher IOP among critical cases, when compared to severe cases, and discrete outer retina changes 80 days after COVID-19 infection. No sign of uveitis was found.

Reference

<https://www.nature.com/articles/s41598-021-90482-2>

Identification of risk groups for mental disorders, headache and oral behaviors in adults during the COVID-19 pandemic

Abstract

The dramatically changing situation during COVID-19 pandemic, is anticipated to provoke psycho-emotional disturbances and somatization arising from the current epidemiological situation that will become a significant problem for global and regional healthcare systems. The aim of this study was to identify the predictors, risk factors and factors associated with mental disorders, headache and potentially stress-modulated parafunctional oral behaviors among the adult residents of North America and Europe as indirect health effects of the COVID-19 pandemic. This may help limit the long-term effects of this and future global pandemic crises. The data were collected from 1642 respondents using an online survey. The results demonstrated increased levels of anxiety, depression, headache and parafunctional oral behaviors during the COVID-19 pandemic in both North American and European residents. The results of this study facilitated the definition of the group most predicted to experience the aforementioned secondary effects of the pandemic. This group included females younger than 28.5 years old, especially those who were single, less well educated and living in Europe. In case of this and other global crises this will allow faster defining the most vulnerable groups and providing rapid and more targeted intervention.

Reference

<https://www.nature.com/articles/s41598-021-90566-z>

Spatiotemporal contact density explains the disparity of COVID-19 spread in urban neighborhoods

Abstract

The rapid early spread of COVID-19 in the US was experienced very differently by different socioeconomic groups and business industries. In this study, aggregate mobility patterns of New York City and Chicago was studied to identify the relationship between the amount of interpersonal contact between people in urban neighborhoods and the disparity in the growth of positive cases among these groups. An aggregate spatiotemporal contact density index (CDI) was introduced to measure the strength of

this interpersonal contact using mobility data collected from mobile phones, and combine it with social distancing metrics to show its effect on positive case growth. With the help of structural equations modeling, we find that the effect of CDI on case growth was consistently positive and that it remained consistently higher in lower-income neighborhoods, suggesting a causal path of income on case growth *via* CDI. Using the CDI, schools and restaurants are identified as high contact density industries, and the estimation suggests that implementing specific mobility restrictions on these point-of-interest categories is most effective. This analysis can be useful in providing insights for government officials targeting specific population groups and businesses to reduce infection spread as reopening efforts continue to expand across the nation.

Reference

<https://www.nature.com/articles/s41598-021-90483-1>

Evolution of disease transmission during the COVID-19 pandemic: Patterns and determinants

Abstract

Epidemic models are being used by governments to inform public health strategies to reduce the spread of SARS-CoV-2. They simulate potential scenarios by manipulating model parameters that control processes of disease transmission and recovery. However, the validity of these parameters is challenged by the uncertainty of the impact of public health interventions on disease transmission, and the forecasting accuracy of these models is rarely investigated during an outbreak. A stochastic transmission model was fitted on reported cases, recoveries and deaths associated with SARS-CoV-2 infection across 101 countries. The dynamics of disease transmission was represented in terms of the daily effective reproduction number (\mathcal{R}_t). The relationship between public health interventions and \mathcal{R}_t was explored, firstly using a hierarchical clustering algorithm on initial \mathcal{R}_t patterns, and secondly computing the time-lagged cross correlation among the daily number of policies implemented, \mathcal{R}_t , and daily incidence counts in subsequent months. The impact of updating \mathcal{R}_t every time a prediction is made on the forecasting accuracy of the model was investigated. We identified 5 groups of countries with distinct transmission patterns during the first 6 months of the pandemic. Early adoption of social distancing measures and a shorter

gap between interventions were associated with a reduction on the duration of outbreaks. The lagged correlation analysis revealed that increased policy volume was associated with lower future $\langle R_t \rangle$ (75 days lag), while a lower $\langle R_t \rangle$ was associated with lower future policy volume (102 days lag). Lastly, the outbreak prediction accuracy of the model using dynamically updated $\langle R_t \rangle$ produced an average AUROC of 0.72 (0.708, 0.723) compared to 0.56 (0.555, 0.568) when $\langle R_t \rangle$ was kept constant. Monitoring the evolution of $\langle R_t \rangle$ during an epidemic is an important complementary piece of information to reported daily counts, recoveries and deaths, since it provides an early signal of the efficacy of containment measures. Using updated $\langle R_t \rangle$ values produces significantly better predictions of future outbreaks. Our results found variation in the effect of early public health interventions on the evolution of $\langle R_t \rangle$ over time and across countries, which could not be explained solely by the timing and number of the adopted interventions.

Reference

<https://www.nature.com/articles/s41598-021-90347-8>

Impact of US vaccination strategy on COVID-19 wave dynamics

Abstract

The epidemic Renormalization Group (eRG) framework was employed to understand, reproduce and predict the COVID-19 pandemic diffusion across the US. The human mobility across different geographical US divisions is modelled *via* open source flight data alongside the impact of social distancing for each such division. The impact of the vaccination strategy was analyzed on the current pandemic wave dynamics in the US. We observe that the ongoing vaccination campaign will not impact the current pandemic wave and therefore strict social distancing measures must still be enacted. To curb the current and the next waves the results indisputably show that vaccinations alone are not enough and strict social distancing measures are required until sufficient immunity is achieved. The results are essential for a successful vaccination strategy in the US.

Reference

<https://www.nature.com/articles/s41598-021-90539-2>

The efficacy and safety of Favipiravir in treatment of COVID-19: A systematic review and meta-analysis of clinical trials

Abstract

The novel coronavirus outbreak began in late December 2019 and rapidly spread worldwide, critically impacting public health systems. A number of already approved and marketed drugs are being tested for repurposing, including Favipiravir. It was aimed to investigate the efficacy and safety of Favipiravir in treatment of COVID-19 patients through a systematic review and meta-analysis. This systematic review and meta-analysis were reported in accordance with the PRISMA statement. The protocol was registered in the PROSPERO (CRD42020180032). All clinical trials which addressed the safety and efficacy of Favipiravir in comparison to other control groups for treatment of patients with confirmed infection with SARS-CoV2 were included. The electronic databases were searched including LitCovid/PubMed, Scopus, Web of Sciences, Cochrane, and Scientific Information Database up to 31 December 2020. The risk of bias of the included studies was assessed using Cochrane Collaboration criteria. All analyses were performed using the Comprehensive Meta-Analysis software version 2, and the risk ratio index was calculated. Egger and Begg test was used for assessing publication bias. Nine studies were included in our meta-analysis. The results of the meta-analysis revealed a significant clinical improvement in the Favipiravir group versus the control group during seven days after hospitalization (RR = 1.24, 95% CI: 1.09–1.41; P = 0.001). Viral clearance was more in 14 days after hospitalization in Favipiravir group than control group, but this finding marginally not significant (RR = 1.11, 95% CI: 0.98–1.25; P = 0.094). Requiring supplemental oxygen therapy in the Favipiravir group was 7% less than the control group, (RR = 0.93, 95% CI: 0.67–1.28; P = 0.664). Transferred to ICU and adverse events were not statistically different between two groups. The mortality rate in the Favipiravir group was approximately 30% less than the control group, but this finding not statistically significant. Favipiravir possibly exerted no significant beneficial effect in the term of mortality in the general group of patients with mild to moderate COVID-19. We should consider that perhaps the use of antiviral once the patient has symptoms is too late and this would explain their low efficacy in the clinical setting.

Reference

<https://www.nature.com/articles/s41598-021-90551-6>

A method for the rational selection of drug repurposing candidates from multimodal knowledge harmonization

Abstract

The SARS-CoV-2 pandemic has challenged researchers at a global scale. The scientific community's massive response has resulted in a flood of experiments, analyses, hypotheses, and publications, especially in the field of drug repurposing. However, many of the proposed therapeutic compounds obtained from SARS-CoV-2 specific assays are not in agreement and thus demonstrate the need for a singular source of COVID-19 related information from which a rational selection of drug repurposing candidates can be made. In this paper, the COVID-19 PHARMACOME was presented, which is a comprehensive drug-target-mechanism graph generated from a compilation of 10 separate disease maps and sources of experimental data focused on SARS-CoV-2/COVID-19 pathophysiology. By applying the systematic approach, it is able to predict the synergistic effect of specific drug pairs, such as Remdesivir and Thioguanosine or Nelfinavir and Raloxifene, on SARS-CoV-2 infection. Experimental validation of the results demonstrates that the graph can be used to not only explore the involved mechanistic pathways, but also to identify novel combinations of drug repurposing candidates.

Reference

<https://www.nature.com/articles/s41598-021-90296-2>

COVID-19-associated *Aspergillus tracheobronchitis*: The interplay between viral tropism, host defence, and fungal invasion

Abstract

Invasive pulmonary aspergillosis is emerging as a secondary infection in patients with COVID-19, which can present as alveolar disease, airway disease (i.e., invasive *Aspergillus tracheobronchitis*), or both. Histopathology of invasive *Aspergillus tracheobronchitis* in patients with severe COVID-19 confirms tracheal ulcers with tissue

invasion of *Aspergillus hyphae* but without angioinvasion, which differs from patients with severe influenza, where early angioinvasion is observed. It was argued that aggregation of predisposing factors (eg, factors that are defined by the European Organisation for Research and Treatment of Cancer and Mycoses Study Group Education and Research Consortium or genetic polymorphisms), viral factors (eg, tropism and lytic effects), immune defence factors, and effects of concomitant therapies will determine whether and when the angioinvasion threshold is reached. Management of invasive *Aspergillus tracheobronchitis* should include reducing viral lytic effects, rebalancing immune dysregulation, and systemic and local antifungal therapy. Future study designs should involve approaches that aim to develop improved diagnostics for tissue invasion and airways involvement and identify the immune status of the patient to guide personalised immunotherapy.

Reference

[https://www.thelancet.com/journals/lanres/article/PIIS2213-2600\(21\)00138-7/fulltext](https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00138-7/fulltext)

Publication Date: May 25, 2021

Tackling COVID-19 with neutralizing monoclonal antibodies

Abstract

Monoclonal antibodies (mAbs) have revolutionized the treatment of several human diseases, including cancer, autoimmunity and inflammatory conditions and represent a new frontier for the treatment of infectious diseases. In the last twenty years, innovative methods have allowed the rapid isolation of mAbs from convalescent subjects, humanized mice or libraries assembled in vitro and have proven that mAbs can be effective countermeasures against emerging pathogens. During the past year, an unprecedentedly large number of mAbs have been developed to fight COVID-19. Lessons learned from this pandemic will pave the way for the development of more mAb-based therapeutics for other infectious diseases. Here, we provide an overview of SARS-CoV-2 neutralizing mAbs, including their origin, specificity, structure, antiviral and immunological mechanisms of action, resistance to circulating variants as well as a snapshot of the clinical trials of approved or late-stage mAb therapeutics.

Reference

[https://www.cell.com/cell/fulltext/S0092-8674\(21\)00602-4](https://www.cell.com/cell/fulltext/S0092-8674(21)00602-4)

An external validation of the QCovid risk prediction algorithm for risk of mortality from COVID-19 in adults: A national validation cohort study in England

Abstract

Background: Public policy measures and clinical risk assessments relevant to COVID-19 need to be aided by risk prediction models that are rigorously developed and validated. We aimed to externally validate a risk prediction algorithm (QCovid) to estimate mortality outcomes from COVID-19 in adults in England.

Methods: A population-based cohort study was done using the UK Office for National Statistics Public Health Linked Data Asset, a cohort of individuals aged 19–100 years, based on the 2011 census and linked to Hospital Episode Statistics, the General Practice Extraction Service data for pandemic planning and research, and radiotherapy and systemic chemotherapy records. The primary outcome was time to COVID-19 death, defined as confirmed or suspected COVID-19 death as per death certification. Two periods were used: (1) Jan 24 to April 30, 2020, and (2) May 1 to July 28, 2020. We assessed the performance of the QCovid algorithms using measures of discrimination and calibration. Using predicted 90-day risk of COVID-19 death, r^2 values were calculated, Brier scores, and measures of discrimination and calibration with corresponding 95% CIs over the two time periods.

Findings: 34 897 648 Adults aged 19–100 years resident in England, were included. 26 985 (0·08%) COVID-19 deaths occurred during the first period and 13 177 (0·04%) during the second. The algorithms had good discrimination and calibration in both periods. In the first period, they explained 77·1% (95% CI 76·9–77·4) of the variation in time to death in men and 76·3% (76·0–76·6) in women. The D statistic was 3·761 (3·732–3·789) for men and 3·671 (3·640–3·702) for women and Harrell's C was 0·935 (0·933–0·937) for men and 0·945 (0·943–0·947) for women. Similar results were obtained for the second time period. In the top 5% of patients with the highest predicted risks of death, the sensitivity for identifying deaths in the first period was 65·94% for men and 71·67% for women.

Interpretation: The QCovid population-based risk algorithm performed well, showing high levels of discrimination for COVID-19 deaths in men and women for both time periods. QCovid has the potential to be dynamically updated as the pandemic evolves and, therefore, has potential use in guiding national policy.

Reference

[https://www.thelancet.com/journals/landig/article/PIIS2589-7500\(21\)00080-7/fulltext](https://www.thelancet.com/journals/landig/article/PIIS2589-7500(21)00080-7/fulltext)

Estimating infectiousness throughout SARS-CoV-2 infection course

Abstract

Two elementary parameters for quantifying viral infection and shedding are viral load and whether samples yield a replicating virus isolate in cell culture. 25,381 German SARS-CoV-2 cases were examined, including 6110 from test centres attended by pre-symptomatic, asymptomatic, and mildly-symptomatic (PAMS) subjects, 9519 who were hospitalised, and 1533 B.1.1.7 lineage infections. The youngest had mean log₁₀ viral load 0.5 (or less) lower than older subjects and an estimated ~78% of the peak cell culture replication probability, due in part to smaller swab sizes and unlikely to be clinically relevant. Viral loads above 109 copies per swab were found in 8% of subjects, one-third of whom were PAMS, with mean age 37.6. We estimate 4.3 days from onset of shedding to peak viral load (8.1) and cell culture isolation probability (0.75). B.1.1.7 subjects had mean log₁₀ viral load 1.05 higher than non-B.1.1.7, with estimated cell culture replication probability 2.6 times higher.

Reference

<https://science.sciencemag.org/content/early/2021/05/24/science.abi5273>

Publication Date: May 24, 2021

An infectivity-enhancing site on the SARS-CoV-2 spike protein targeted by antibodies

Abstract

Antibodies against the receptor-binding-domain of the SARS-CoV-2 spike protein prevent SARS-CoV-2 infection. However, the effects of antibodies against other spike

protein domains are largely unknown. Here, a series of anti-spike monoclonal antibodies from COVID-19 patients were screened, and found that some of antibodies against the *N*-terminal-domain (NTD) induced the open conformation of receptor binding domain (RBD) and thus enhanced the binding capacity of the spike protein to ACE2 and infectivity of SARS-CoV-2. Mutational analysis revealed that all the infectivity-enhancing antibodies recognized a specific site on the NTD. Structural analysis demonstrated that all the infectivity-enhancing antibodies bound to NTD in a similar manner. The antibodies against this infectivity-enhancing site were detected at high levels in severe patients. Moreover, we identified antibodies against the infectivity-enhancing site in uninfected donors, albeit at a lower frequency. These findings demonstrate that not only neutralizing antibodies but also enhancing antibodies are produced during SARS-CoV-2 infection.

Reference

[https://www.cell.com/cell/fulltext/S0092-8674\(21\)00662-0](https://www.cell.com/cell/fulltext/S0092-8674(21)00662-0)

Global analysis of protein-RNA interactions in SARS-CoV-2 infected cells reveals key regulators of infection

Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes COVID-19. SARS-CoV-2 relies on cellular RNA-binding proteins (RBPs) to replicate and spread, although which RBPs control its life cycle remains largely unknown. Here, a multi-omic approach was employed to identify systematically and comprehensively the cellular and viral RBPs that are involved in SARS-CoV-2 infection. It was revealed that SARS-CoV-2 infection profoundly remodels the cellular RNA-bound proteome, which includes wide-ranging effects on RNA metabolic pathways, non-canonical RBPs and antiviral factors. Moreover, we apply a new method to identify the proteins that directly interact with viral RNA, uncovering dozens of cellular RBPs and six viral proteins. Amongst them, several components of the tRNA ligase complex, which were shown to regulate SARS-CoV-2 infection. Furthermore, we discover that available drugs targeting host RBPs that interact with SARS-CoV-2 RNA inhibit infection. Collectively, the results uncover a new universe of host-virus interactions with potential for new antiviral therapies against COVID-19.

Reference

[https://www.cell.com/molecular-cell/fulltext/S1097-2765\(21\)00407-X](https://www.cell.com/molecular-cell/fulltext/S1097-2765(21)00407-X)

Binding and molecular basis of the bat coronavirus RaTG13 virus to ACE-2 in humans and other species

Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been spreading worldwide and causing a global pandemic. Bat-origin RaTG13 is currently the most phylogenetically related virus. Here, the complex structure of RaTG13 receptor binding domain (RBD) with human ACE2 (hACE2) were obtained, and further evaluated the binding of RaTG13 RBD to 24 additional ACE2 orthologs. By substituting residues in RaTG13 RBD with their counterparts in SARS-CoV-2 RBD, we found that residue 501, the major position found in VOCs 501Y.V1/V2/V3, plays a key role in determining the potential host range of RaTG13. It was also found that SARS-CoV-2 could induce strong cross-reactive antibodies to RaTG13 and identified a SARS-CoV-2 MAb, CB6, that could cross-neutralize RaTG13 pseudovirus. These results elucidate the receptor binding and host-adaption mechanisms of RaTG13 and emphasize the importance of continuous surveillance of coronaviruses (CoVs) carried by animal reservoirs to prevent another spill-over of CoVs.

Reference

[https://www.cell.com/cell/fulltext/S0092-8674\(21\)00661-9](https://www.cell.com/cell/fulltext/S0092-8674(21)00661-9)

A population-based analysis of the longevity of SARS-CoV-2 antibody seropositivity in the United States

Abstract

Background: This cross-sectional study aimed to track population-based SARS-CoV-2 antibody seropositivity duration across the United States using observational data from a national clinical laboratory registry of patients tested by nucleic acid amplification (NAAT) and serologic assays. Knowledge of antibody seropositivity and its duration may help dictate post-pandemic planning.

Methods: Using assays to detect antibodies to either nucleocapsid (N) or spike (S) proteins performed on specimens from 39,086 individuals with confirmed positive COVID-19 by reverse transcription-polymerase chain reaction (RT-PCR) from March 2020 to January 2021, we analyzed nationwide seropositivity rates of IgG up to 300 days following patients' initial positive NAAT test. Linear regression identified trends in seropositivity rates and logistic regression tested positive predictability by age, sex, assay type and days post-infection.

Findings: Seropositivity of IgG antibodies to both SARS-CoV-2 S and N-proteins followed a linear trend reaching approximately 90% positivity at 21 days post-index. The rate of N-protein seropositivity declined at a sharper rate, decaying to 68.2% [95% CI: 63.1–70.8%] after 293 days, while S-antibody seropositivity maintained a rate of 87.8% [95% CI: 86.3–89.1%] through 300 days. In addition to antigen type and the number of days post-positive PCR, age and gender were also significant factors in seropositivity prediction, with those under 65 years of age showing a more sustained seropositivity rate.

Interpretation: Observational data from a national clinical laboratory, though limited by an epidemiological view of the U.S. population, offer an encouraging timeline for the development and sustainability of antibodies up to ten months from natural infection and could inform post-pandemic planning.

Reference

[https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370\(21\)00182-6/fulltext](https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00182-6/fulltext)

Comparing infectivity and virulence of emerging SARS-CoV-2 variants in Syrian hamsters

Abstract

Background: Within one year after its emergence, more than 108 million people acquired SARS-CoV-2 and almost 2.4 million succumbed to COVID-19. New SARS-CoV-2 variants of concern (VoC) are emerging all over the world, with the threat of being more readily transmitted, being more virulent, or escaping naturally acquired and vaccine-induced immunity. At least three major prototypic VoC have been identified, i.e. the United Kingdom, UK (B.1.1.7), South African (B.1.351) and Brazilian (B.1.1.28.1)

variants. These are replacing formerly dominant strains and sparking new COVID-19 epidemics.

Methods: The effect of infection was studied with prototypic VoC from both B.1.1.7 and B.1.351 variants in female Syrian golden hamsters to assess their relative infectivity and virulence in direct comparison to two basal SARS-CoV-2 strains isolated in early 2020.

Findings: A very efficient infection of the lower respiratory tract of hamsters by these VoC is observed. In line with clinical evidence from patients infected with these VoC, no major differences in disease outcome were observed as compared to the original strains as was quantified by (i) histological scoring, (ii) micro-computed tomography, and (iii) analysis of the expression profiles of selected antiviral and pro-inflammatory cytokine genes. Noteworthy however, in hamsters infected with VoC B.1.1.7, a particularly strong elevation of proinflammatory cytokines was detected.

Interpretation: Relevant preclinical infection models were established that will be pivotal to assess the efficacy of current and future vaccine(s) (candidates) as well as therapeutics (small molecules and antibodies) against two important SARS-CoV-2 VoC.

Reference

[https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964\(21\)00196-1/fulltext](https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(21)00196-1/fulltext)

Publication Date: May 23, 2021

SARS-CoV-2 seroprevalence in the urban population of Qatar: An analysis of antibody testing on a sample of 112,941 individuals

Abstract

The study objective was to assess level of detectable SARS-CoV-2 antibodies in the urban population of Qatar. Antibody testing was performed on residual blood specimens for 112,941 individuals (~10% of Qatar's urban population) attending for routine/other clinical care between May 12-September 9, 2020. Seropositivity was 13.3% (95% CI=13.1-13.6%) and was independently associated with sex, age, nationality, clinical-care encounter type, and testing date. Median optical density (antibody titer) among antibody-positive persons was 27.0 (range=1.0-150.0), with higher values associated

with age, nationality, clinical-care encounter type, and testing date. Seropositivity by nationality was positively-correlated with the likelihood of having higher antibody titers (Pearson correlation coefficient=0.85; 95% CI=0.47-0.96). Less than two in every 10 individuals in Qatar's urban population had detectable antibodies against SARS-CoV-2, suggesting this population is still far from herd immunity and at risk of subsequent infection waves. Higher antibody titer appears to be a biomarker of repeated exposures to the infection.

Reference

[https://www.cell.com/iscience/fulltext/S2589-0042\(21\)00614-3](https://www.cell.com/iscience/fulltext/S2589-0042(21)00614-3)

Publication Date: May 22, 2021

Patient care and clinical outcomes for patients with COVID-19 infection admitted to African high-care or intensive care units (ACCCOS): A multicentre, prospective, observational cohort study

Abstract

Background: There have been insufficient data for African patients with COVID-19 who are critically ill. The African COVID-19 Critical Care Outcomes Study (ACCCOS) aimed to determine which resources, comorbidities, and critical care interventions are associated with mortality in this patient population.

Methods: The ACCCOS study was a multicentre, prospective, observational cohort study in adults (aged 18 years or older) with suspected or confirmed COVID-19 infection who were referred to intensive care or high-care units in 64 hospitals in ten African countries (ie, Egypt, Ethiopia, Ghana, Kenya, Libya, Malawi, Mozambique, Niger, Nigeria, and South Africa). The primary outcome was in-hospital mortality censored at 30 days. We studied the factors (ie, human and facility resources, patient comorbidities, and critical care interventions) that were associated with mortality in these adult patients. This study is registered on ClinicalTrials.gov, NCT04367207.

Findings: From May to December, 2020, 6779 patients were referred to critical care. Of these, 3752 (55.3%) patients were admitted and 3140 (83.7%) patients from 64 hospitals in ten countries participated (mean age 55.6 years; 1890 [60.6%] of 3118

participants were male). The hospitals had a median of two intensivists (IQR 1–4) and pulse oximetry was available to all patients in 49 (86%) of 57 sites. In-hospital mortality within 30 days of admission was 48·2% (95% CI 46·4–50·0; 1483 of 3077 patients). Factors that were independently associated with mortality were increasing age per year (odds ratio 1·03; 1·02–1·04); HIV/AIDS (1·91; 1·31–2·79); diabetes (1·25; 1·01–1·56); chronic liver disease (3·48; 1·48–8·18); chronic kidney disease (1·89; 1·28–2·78); delay in admission due to a shortage of resources (2·14; 1·42–3·22); quick sequential organ failure assessment score at admission (for one factor [1·44; 1·01–2·04], for two factors [2·0; 1·33–2·99], and for three factors [3·66, 2·12–6·33]); respiratory support (high flow oxygenation [2·72; 1·46–5·08]; continuous positive airway pressure [3·93; 2·13–7·26]; invasive mechanical ventilation [15·27; 8·51–27·37]); cardiorespiratory arrest within 24 h of admission (4·43; 2·25–8·73); and vasopressor requirements (3·67; 2·77–4·86). Steroid therapy was associated with survival (0·55; 0·37–0·81). There was no difference in outcome associated with female sex (0·86; 0·69–1·06).

Interpretation: Mortality in critically ill patients with COVID-19 is higher in African countries than reported from studies done in Asia, Europe, North America, and South America. Increased mortality was associated with insufficient critical care resources, as well as the comorbidities of HIV/AIDS, diabetes, chronic liver disease, and kidney disease, and severity of organ dysfunction at admission.

Reference

[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(21\)00441-4/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00441-4/fulltext)

Characteristics and predictors of acute and chronic post-COVID syndrome: A systematic review and meta-analysis

Abstract

Background: A significant proportion of individuals experience lingering and debilitating symptoms following acute COVID-19 infection. The National Institute for Health and Care Excellence (NICE) have coined the persistent cluster of symptoms as post-COVID syndrome. This has been further sub-categorised into acute post-COVID syndrome for symptoms persisting three weeks beyond initial infection and chronic post-COVID syndrome for symptoms persisting beyond twelve weeks. The aim of this review was to

detail the prevalence of clinical features and identify potential predictors for acute and chronic post-COVID syndrome.

Methods: A systematic literature search, with no language restrictions, was performed to identify studies detailing characteristics and outcomes related to survivorship of post-COVID syndrome. The last search was performed on 6 March 2021 and all pre-dating published articles included. A means of proportion meta-analysis was performed to quantify characteristics of acute and chronic post-COVID syndrome. Study quality was assessed with a specific risk of bias tool. PROSPERO Registration: CRD42020222855

Findings: A total of 43 studies met the eligibility criteria; of which, 38 allowed for meta-analysis. Fatigue and dyspnoea were the most prevalent symptoms in acute post-COVID (0·37 and 0·35) and fatigue and sleep disturbance in chronic post-COVID syndrome (0·48 and 0·44), respectively. The available evidence is generally of poor quality, with considerable risk of bias, and are of observational design.

Interpretation: In conclusion, this review highlights that flaws in data capture and interpretation, noted in the uncertainty within our meta-analysis, affect the applicability of current knowledge. Policy makers and researchers must focus on understanding the impact of this condition on individuals and society with appropriate funding initiatives and global collaborative research.

Reference

[https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370\(21\)00179-6/fulltext](https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00179-6/fulltext)

atient care and clinical outcomes for patients with COVID-19 infection admitted to African high-care or intensive care units (ACCCOS): A multicentre, prospective, observational cohort study

Abstract

Background: There have been insufficient data for African patients with COVID-19 who are critically ill. The African COVID-19 Critical Care Outcomes Study (ACCCOS) aimed to determine which resources, comorbidities, and critical care interventions are associated with mortality in this patient population.

Methods: The ACCCOS study was a multicentre, prospective, observational cohort study in adults (aged 18 years or older) with suspected or confirmed COVID-19 infection who were referred to intensive care or high-care units in 64 hospitals in ten African countries (ie, Egypt, Ethiopia, Ghana, Kenya, Libya, Malawi, Mozambique, Niger, Nigeria, and South Africa). The primary outcome was in-hospital mortality censored at 30 days. We studied the factors (ie, human and facility resources, patient comorbidities, and critical care interventions) that were associated with mortality in these adult patients. This study is registered on ClinicalTrials.gov, NCT04367207.

Findings: From May to December, 2020, 6779 patients were referred to critical care. Of these, 3752 (55.3%) patients were admitted and 3140 (83.7%) patients from 64 hospitals in ten countries participated (mean age 55.6 years; 1890 [60.6%] of 3118 participants were male). The hospitals had a median of two intensivists (IQR 1–4) and pulse oximetry was available to all patients in 49 (86%) of 57 sites. In-hospital mortality within 30 days of admission was 48.2% (95% CI 46.4–50.0; 1483 of 3077 patients). Factors that were independently associated with mortality were increasing age per year (odds ratio 1.03; 1.02–1.04); HIV/AIDS (1.91; 1.31–2.79); diabetes (1.25; 1.01–1.56); chronic liver disease (3.48; 1.48–8.18); chronic kidney disease (1.89; 1.28–2.78); delay in admission due to a shortage of resources (2.14; 1.42–3.22); quick sequential organ failure assessment score at admission (for one factor [1.44; 1.01–2.04], for two factors [2.0; 1.33–2.99], and for three factors [3.66, 2.12–6.33]); respiratory support (high flow oxygenation [2.72; 1.46–5.08]; continuous positive airway pressure [3.93; 2.13–7.26]; invasive mechanical ventilation [15.27; 8.51–27.37]); cardiorespiratory arrest within 24 h of admission (4.43; 2.25–8.73); and vasopressor requirements (3.67; 2.77–4.86). Steroid therapy was associated with survival (0.55; 0.37–0.81). There was no difference in outcome associated with female sex (0.86; 0.69–1.06).

Interpretation: Mortality in critically ill patients with COVID-19 is higher in African countries than reported from studies done in Asia, Europe, North America, and South America. Increased mortality was associated with insufficient critical care resources, as well as the comorbidities of HIV/AIDS, diabetes, chronic liver disease, and kidney disease, and severity of organ dysfunction at admission.

Reference

Characteristics and predictors of acute and chronic post-COVID syndrome: A systematic review and meta-analysis

Abstract

Background: A significant proportion of individuals experience lingering and debilitating symptoms following acute COVID-19 infection. The National Institute for Health and Care Excellence (NICE) have coined the persistent cluster of symptoms as post-COVID syndrome. This has been further sub-categorised into acute post-COVID syndrome for symptoms persisting three weeks beyond initial infection and chronic post-COVID syndrome for symptoms persisting beyond twelve weeks. The aim of this review was to detail the prevalence of clinical features and identify potential predictors for acute and chronic post-COVID syndrome.

Methods: A systematic literature search, with no language restrictions, was performed to identify studies detailing characteristics and outcomes related to survivorship of post-COVID syndrome. The last search was performed on 6 March 2021 and all pre-dating published articles included. A means of proportion meta-analysis was performed to quantify characteristics of acute and chronic post-COVID syndrome. Study quality was assessed with a specific risk of bias tool.

Findings: A total of 43 studies met the eligibility criteria; of which, 38 allowed for meta-analysis. Fatigue and dyspnoea were the most prevalent symptoms in acute post-COVID (0·37 and 0·35) and fatigue and sleep disturbance in chronic post-COVID syndrome (0·48 and 0·44), respectively. The available evidence is generally of poor quality, with considerable risk of bias, and are of observational design.

Interpretation: In conclusion, this review highlights that flaws in data capture and interpretation, noted in the uncertainty within the meta-analysis, affect the applicability of current knowledge. Policy makers and researchers must focus on understanding the impact of this condition on individuals and society with appropriate funding initiatives and global collaborative research.

Reference

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Pulmonary stromal expansion and intra-alveolar coagulation are primary causes of COVID-19 death

Abstract

Most COVID-19 victims are old and die from unrelated causes. Here twelve complete autopsies were presented, including two rapid autopsies of young patients where the cause of death was COVID-19 ARDS. The main virus induced pathology was in the lung parenchyma and not in the airways. Most coagulation events occurred in the intra-alveolar and not in the intra-vascular space and the few thrombi were mainly composed of aggregated thrombocytes. The dominant inflammatory response was the massive accumulation of CD163+ macrophages and the disappearance of T killer, NK and B-cells. The virus was replicating in the pneumocytes and macrophages but not in bronchial epithelium, endothelium, pericytes or stromal cells. The lung consolidations were produced by a massive regenerative response, stromal and epithelial proliferation and neovascularization. It was suggested that thrombocyte aggregation inhibition, angiogenesis inhibition and general proliferation inhibition may have a roll in the treatment of advanced COVID-19 ARDS.

Reference

[https://www.cell.com/heliyon/fulltext/S2405-8440\(21\)01237-8](https://www.cell.com/heliyon/fulltext/S2405-8440(21)01237-8)

Publication Date: May 21, 2021

SARS-CoV-2 Human T cell Epitopes: Adaptive immune response against COVID-19

Abstract

Over the past year, numerous studies in the peer reviewed and preprint literature have reported on the virological, epidemiological and clinical characteristics of the coronavirus, SARS-CoV-2. To date, 25 studies have investigated and identified SARS-CoV-2-derived T cell epitopes in humans. Here, these recent studies were reviewed,

how they were performed, and their findings. It was reviewed how epitopes identified throughout the SARS-CoV2 proteome reveal significant correlation between number of epitopes defined and size of the antigen provenance. We also report additional analysis of SARS-CoV-2 human CD4 and CD8 T-cell epitope data compiled from these studies, identifying 1400 different reported SARS-CoV-2 epitopes and revealing discrete immunodominant regions of the virus and epitopes that are more prevalently recognized. This remarkable breadth of epitope repertoire has implications for vaccine design, cross-reactivity and for immune escape by SARS-CoV-2 variants.

Reference

[https://www.cell.com/cell-host-microbe/fulltext/S1931-3128\(21\)00238-9](https://www.cell.com/cell-host-microbe/fulltext/S1931-3128(21)00238-9)

Clinical frailty scale as a point of care prognostic indicator of mortality in COVID-19: A systematic review and meta-analysis

Abstract

Background: COVID-19 has resulted in the largest pandemic experienced since 1918, accounting for over 2 million deaths globally. Frail and older people are at the highest risk of mortality. The main objective of the present research was to quantify the impact of clinical frailty scale (CFS) by increasing severity of frailty and to identify other personal prognostic factors associated with increased mortality from COVID-19.

Methods: This study offers a contemporary systematic review and meta-analysis to analyse the stratified mortality risk by increasing CFS sub-categories (1–3, 4–5 and 6–9). Databases searched included EMBASE, MEDLINE, CAB Abstracts, PsychInfo, and Web of Science with end-search restriction the 18th December 2020. Publications identified via MedRevix were followed up on the 23rd March 2021 in peer-reviewed database search, and citations were updated as published. Prospective and retrospective cohort studies which reported the association between CFS and COVID-19 mortality were included. Thirty-four studies were eligible for systematic review and seventeen for meta-analysis, with 81–87% (I²) heterogeneity.

Findings: All studies [N: 34] included patients from a hospital setting, comprising a total of 18,042 patients with mean age 72.8 (Min: 56; Max: 86). The CFS 4–5 patient group had significantly increased mortality when compared to patients with CFS 1–3 [(RE) OR

1.95 (1.32 (95% CI), 2.87 (95% CI)); I2 81%; p = 0.0008]. Furthermore, CFS 6–9 patient group displayed an even more noticeable mortality increase when compared to patients with CFS 1–3 [(RE) OR 3.09 (2.03, 4.71); I2 87%; p<0.0001]. Generic inverse variance analysis of adjusted hazard ratio among included studies highlighted that CFS (p = 0.0001), male gender (p = 0.0009), National Early Warning Score (p = 0.0001), Ischaemic Heart Disease (IHD) (p = 0.07), Hypertension (HT) (p<0.0001), and Chronic Kidney Disease (CKD) (p = 0.0009) were associated with increased COVID-19 mortality.

Interpretation: The findings suggest a differential stratification of CFS scores in the context of COVID-19 infection, in which CFS 1–3 patients may be considered at lower risk, CFS 4–5 at moderate risk, and CFS 6–9 at high risk of mortality regardless of age. Overall, our study not only aims to alert clinicians of the value of CFS scores, but also highlight the multiple dimensions to consider such as age, gender and co-morbidities, even among moderately frail patients in relation to COVID-19 mortality.

Reference

[https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370\(21\)00176-0/fulltext](https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00176-0/fulltext)

Peripheral and lung resident memory T cell responses against SARS-CoV-2

Abstract

Resident memory T cells (TRM) positioned within the respiratory tract are probably required to limit SARS-CoV-2 spread and COVID-19. Importantly, TRM are mostly non-recirculating, which reduces the window of opportunity to examine these cells in the blood as they move to the lung parenchyma. Here, we identify circulating virus-specific T cell responses during acute infection with functional, migratory and apoptotic patterns modulated by viral proteins and associated with clinical outcome. Disease severity is associated predominantly with IFN γ and IL-4 responses, increased responses against S peptides and apoptosis, whereas non-hospitalized patients have increased IL-12p70 levels, degranulation in response to N peptides and SARS-CoV-2-specific CCR7+ T cells secreting IL-10. In convalescent patients, lung-TRM are frequently detected even 10 months after initial infection, in which contemporaneous blood does not reflect tissue-resident profiles. The study highlights a balanced anti-inflammatory antiviral

response associated with a better outcome and persisting TRM cells as important for future protection against SARS-CoV-2 infection.

Reference

<https://www.nature.com/articles/s41467-021-23333-3>

Clinical frailty scale as a point of care prognostic indicator of mortality in COVID-19: A systematic review and meta-analysis

Abstract

Background: COVID-19 has resulted in the largest pandemic experienced since 1918, accounting for over 2 million deaths globally. Frail and older people are at the highest risk of mortality. The main objective of the present research was to quantify the impact of clinical frailty scale (CFS) by increasing severity of frailty and to identify other personal prognostic factors associated with increased mortality from COVID-19.

Methods: This study offers a contemporary systematic review and meta-analysis to analyse the stratified mortality risk by increasing CFS sub-categories (1–3, 4–5 and 6–9). Databases searched included EMBASE, MEDLINE, CAB Abstracts, PsychInfo, and Web of Science with end-search restriction the 18th December 2020. Publications identified via MedRevix were followed up on the 23rd March 2021 in peer-reviewed database search, and citations were updated as published. Prospective and retrospective cohort studies which reported the association between CFS and COVID-19 mortality were included. Thirty-four studies were eligible for systematic review and seventeen for meta-analysis, with 81–87% (I²) heterogeneity.

Findings: All studies [N: 34] included patients from a hospital setting, comprising a total of 18,042 patients with mean age 72.8 (Min: 56; Max: 86). The CFS 4–5 patient group had significantly increased mortality when compared to patients with CFS 1–3 [(RE) OR 1.95 (1.32 (95% CI), 2.87 (95% CI)); I² 81%; p = 0.0008]. Furthermore, CFS 6–9 patient group displayed an even more noticeable mortality increase when compared to patients with CFS 1–3 [(RE) OR 3.09 (2.03, 4.71); I² 87%; p<0.0001]. Generic inverse variance analysis of adjusted hazard ratio among included studies highlighted that CFS (p = 0.0001), male gender (p = 0.0009), National Early Warning Score (p = 0.0001), Ischaemic Heart Disease (IHD) (p = 0.07), Hypertension (HT) (p<0.0001), and Chronic

Kidney Disease (CKD) ($p = 0.0009$) were associated with increased COVID-19 mortality.

Interpretation: The findings suggest a differential stratification of CFS scores in the context of COVID-19 infection, in which CFS 1–3 patients may be considered at lower risk, CFS 4–5 at moderate risk, and CFS 6–9 at high risk of mortality regardless of age. Overall, our study not only aims to alert clinicians of the value of CFS scores, but also highlight the multiple dimensions to consider such as age, gender and co-morbidities, even among moderately frail patients in relation to COVID-19 mortality.

Reference

[https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370\(21\)00176-0/fulltext](https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00176-0/fulltext)

Severe T-cell hyporeactivity in ventilated COVID-19 patients correlates with prolonged virus persistence and poor outcomes

Abstract

Coronavirus disease 2019 (COVID-19) can lead to pneumonia and hyperinflammation. Here we show a sensitive method to measure polyclonal T cell activation by downstream effects on responder cells like basophils, plasmacytoid dendritic cells, monocytes and neutrophils in whole blood. A clear T cell hyporeactivity in hospitalized COVID-19 patients was reported that is pronounced in ventilated patients, associated with prolonged virus persistence and reversible with clinical recovery. COVID-19-induced T cell hyporeactivity is T cell extrinsic and caused by plasma components, independent of occasional immunosuppressive medication of the patients. Monocytes respond stronger in males than females and IL-2 partially restores T cell activation. Downstream markers of T cell hyporeactivity are also visible in fresh blood samples of ventilated patients. Based on our data we developed a score to predict fatal outcomes and identify patients that may benefit from strategies to overcome T cell hyporeactivity.

Reference

<https://www.nature.com/articles/s41467-021-23334-2>

Characteristics of mental health implications and plasma metabolomics in patients recently recovered from COVID-19

Abstract

This study aimed to explore the associations between cerebral white matter (WM) alterations, mental health status, and metabolism in recovered COVID-19 patients. 28 Recovered COVID-19 patients and 27 healthy controls were included between April 2020 and June 2020. Demographic data, the mental health scores, diffusion-tensor imaging (DTI) data, and plasma metabolomics were collected and compared between the two groups. Tract-based spatial statistics and graph theory approaches were used for DTI data analysis. Untargeted metabolomics analysis of the plasma was performed. Correlation analyses were performed between these characteristics. Recovered COVID-19 patients showed decreased fractional anisotropy, increased mean diffusivity and radial diffusivity values in widespread brain regions, and significantly lower global efficiency, longer shortest path length, and less nodal local efficiency in superior occipital gyrus (all, $P < 0.05$, Bonferroni corrected). The results also demonstrated significantly different plasma metabolic profiling in recovered COVID-19 patients even at 3 months after their hospital discharge, which was mainly related to purine pathways, amino acids, lipids, and amine metabolism. Certain regions with cerebral WM alterations in the recovered patients showed significant correlations with different metabolites and the mental health scores. We observed multiple alterations in both WM integrity and plasma metabolomics that may explain the deteriorated mental health of recovered COVID-19 patients. These findings may provide potential biomarkers for the mental health evaluation for the recovered COVID-19 patients and potential targets for novel therapeutics.

Reference

<https://www.nature.com/articles/s41398-021-01426-3>

Point-of-care lung ultrasound in COVID-19 patients: Inter- and intra-observer agreement in a prospective observational study

Abstract

With an urgent need for bedside imaging of coronavirus disease 2019 (COVID-19), this study's main goal was to assess inter- and intraobserver agreement in lung ultrasound (LUS) of COVID-19 patients. In this single-center study we prospectively acquired and evaluated 100 recorded ten-second cine-loops in confirmed COVID-19 intensive care unit (ICU) patients. All loops were rated by ten observers with different subspecialty backgrounds for four times by each observer (400 loops overall) in a random sequence using a web-based rating tool. Inter- and intraobserver variability for specific pathologies and a semiquantitative LUS score were analyzed. Interobserver agreement for both, identification of specific pathologies and assignment of LUS scores was fair to moderate (e.g., LUS score 1 Fleiss' $\kappa=0.27$; subpleural consolidations Fleiss' $\kappa=0.59$). Intraobserver agreement was mostly moderate to substantial with generally higher agreement for more distinct findings (e.g., lowest LUS score 0 vs. highest LUS score 3 (median Fleiss' $\kappa=0.71$ vs. 0.79) or air bronchograms (median Fleiss' $\kappa=0.72$)). Intraobserver consistency was relatively low for intermediate LUS scores (e.g. LUS Score 1 median Fleiss' $\kappa=0.52$). We therefore conclude that more distinct LUS findings (e.g., air bronchograms, subpleural consolidations) may be more suitable for disease monitoring, especially with more than one investigator and that training material used for LUS in point-of-care ultrasound (POCUS) should pay refined attention to areas such as B-line quantification and differentiation of intermediate LUS scores.

Reference

<https://www.nature.com/articles/s41598-021-90153-2>

A clinical staging proposal of the disease course over time in non-severe patients with coronavirus disease 2019

Abstract

Information on the clinical staging of coronavirus disease 2019 (COVID-19) is still limited. This study aimed to propose a clinical staging proposal of the disease course in non-severe patients with COVID-19. In this retrospective study, 108 non-severe patients

with COVID-19 were grouped according to the duration from symptoms onset to hospital admission: ≤ 1 week, > 1 to 2 weeks, > 2 to 3 weeks, > 3 to 5 weeks, respectively. The dynamic changes of clinical signs were profiled across the four groups. A clinical staging proposal of the disease course over time was proposed from the perspective of the interaction between the virus and host. The prodromal phase, characterized by pneumonia, significant lymphopenia, and slightly elevated inflammatory markers, occurred in the first week after symptoms onset. In the second week, all the hematological and inflammatory markers were at the peak or bottom. Meanwhile, progressive pneumonia as well as the secondary damage of other organs (e.g. cardiac damage, coagulopathy, etc.) was significant during this period, making the disease progress into the apparent manifestation phase. In the third week, the improvement of the majority of clinical signs accompanied by a relatively high degree of inflammatory response defined the remission phase. After 3 weeks, patients were in the convalescent phase, in which all the indicators were maintained at a relatively normal level. It was concluded that the disease course over time in non-severe patients with COVID-19 could be divided into four phases: the prodromal phase (in the first week), the apparent manifestation phase (in the second week), the remission phase (in the third week), and the convalescent phase (after 3 weeks), respectively. In clinical practice, tailored therapies should be considered seriously in different stages of the disease course.

Reference

<https://www.nature.com/articles/s41598-021-90111-y>

Prevalence of SARS-CoV-2 antibodies in France: Results from nationwide serological surveillance

Abstract

Assessment of the cumulative incidence of SARS-CoV-2 infections is critical for monitoring the course and extent of the COVID-19 epidemic. Here, estimated seroprevalence was reported in the French population and the proportion of infected individuals who developed neutralising antibodies at three points throughout the first epidemic wave. Testing 11,000 residual specimens for anti-SARS-CoV-2 IgG and neutralising antibodies, we find nationwide seroprevalence of 0.41% (95% CI: 0.05–

0.88) mid-March, 4.14% (95% CI: 3.31–4.99) mid-April and 4.93% (95% CI: 4.02–5.89) mid-May 2020. Approximately 70% of seropositive individuals have detectable neutralising antibodies. Infection fatality rate is 0.84% (95% CI: 0.70–1.03) and increases exponentially with age. These results confirm that the nationwide lockdown substantially curbed transmission and that the vast majority of the French population remained susceptible to SARS-CoV-2 in May 2020. The study shows the progression of the first epidemic wave and provides a framework to inform the ongoing public health response as viral transmission continues globally.

Reference

<https://www.nature.com/articles/s41467-021-23233-6>

Flow cytometry detection of sustained humoral immune response (IgG + IgA) against native spike glycoprotein in asymptomatic/mild SARS-CoV-2 infection

Abstract

SARS-CoV-2 is the virus that causes the disease called COVID-19, which has caused the worst pandemic of the century. Both, to know the immunological status of general population and to evaluate the efficacy of the vaccination process that is taking place around the world, serological tests represent a key tool. Classic serological tests, based on colorimetric techniques, such as ELISA or CLIA, continue to be the most widely used option. However, a real improvement in results is still needed. We developed a highly sensitive and specific FCM assay that allows the detection of IgG and IgA antibodies, directed against the native and functional S-protein of SARS-CoV-2 exposed on the membrane of a transfected cell line, up to 8 months after infection.

Reference

<https://www.nature.com/articles/s41598-021-90054-4>

Humoral immune response to circulating SARS-CoV-2 variants elicited by inactivated and RBD-subunit vaccines

Abstract

SARS-CoV-2 variants could induce immune escape by mutations on the receptor-binding domain (RBD) and N-terminal domain (NTD). Here the humoral immune

response was reported to circulating SARS-CoV-2 variants, such as 501Y.V2 (B.1.351), of the plasma and neutralizing antibodies (NAbs) elicited by CoronaVac (inactivated vaccine), ZF2001 (RBD-subunit vaccine) and natural infection. Among 86 potent NAbs identified by high-throughput single-cell VDJ sequencing of peripheral blood mononuclear cells from vaccinees and convalescents, near half anti-RBD NAbs showed major neutralization reductions against the K417N/E484K/N501Y mutation combination, with E484K being the dominant cause. VH3-53/VH3-66 recurrent antibodies respond differently to RBD variants, and K417N compromises the majority of neutralizing activity through reduced polar contacts with complementarity determining regions. In contrast, the 242–244 deletion (242–244 Δ) would abolish most neutralization activity of anti-NTD NAbs by interrupting the conformation of NTD antigenic supersite, indicating a much less diversity of anti-NTD NAbs than anti-RBD NAbs. Plasma of convalescents and CoronaVac vaccinees displayed comparable neutralization reductions against pseudo- and authentic 501Y.V2 variants, mainly caused by E484K/N501Y and 242–244 Δ , with the effects being additive. Importantly, RBD-subunit vaccinees exhibit markedly higher tolerance to 501Y.V2 than convalescents, since the elicited anti-RBD NAbs display a high diversity and are unaffected by NTD mutations. Moreover, an extended gap between the third and second doses of ZF2001 leads to better neutralizing activity and tolerance to 501Y.V2 than the standard three-dose administration. Together, these results suggest that the deployment of RBD-vaccines, through a third-dose boost, may be ideal for combating SARS-CoV-2 variants when necessary, especially for those carrying mutations that disrupt the NTD supersite.

Reference

<https://www.nature.com/articles/s41422-021-00514-9>

Antibody avidity, persistence, and response to antigen recall: comparison of vaccine adjuvants

Abstract

Differences in innate immune ‘imprinting’ between vaccine adjuvants may mediate dissimilar effects on the quantity/quality of persisting adaptive responses. Antibody avidity maturation, antibody/memory B cell/CD4⁺ T cell response durability, and recall responses to non-adjuvanted fractional-dose antigen administered 1-year post-

immunization (Day [D]360), between hepatitis B vaccines containing Adjuvant System (AS)01B, AS01E, AS03, AS04, or Alum (NCT00805389) were compared. Both the antibody and B cell levels ranked similarly (AS01B/E/AS03 > AS04 > Alum) at peak response, at D360, and following their increases post-antigen recall (D390). Proportions of high-avidity antibodies increased post-dose 2 across all groups and persisted at D360, but avidity maturation appeared to be more strongly promoted by AS vs. Alum. Post-antigen recall, frequencies of subjects with high-avidity antibodies increased only markedly in the AS groups. Among the AS, total antibody responses were lowest for AS04. However, proportions of high-avidity antibodies were similar between groups, suggesting that MPL in AS04 contributes to avidity maturation. Specific combinations of immunoenhancers in the AS, regardless of their individual nature, increase antibody persistence and avidity maturation.

Reference

<https://www.nature.com/articles/s41541-021-00337-0>

SARS-CoV-2 Human T cell Epitopes: Adaptive immune response against COVID-19

Abstract

Over the past year, numerous studies in the peer reviewed and preprint literature have reported on the virological, epidemiological and clinical characteristics of the coronavirus, SARS-CoV-2. To date, 25 studies have investigated and identified SARS-CoV-2-derived T cell epitopes in humans. Here, these recent studies were reviewed, how they were performed, and their findings. It was also reviewed how epitopes identified throughout the SARS-CoV2 proteome reveal significant correlation between number of epitopes defined and size of the antigen provenance. Additional analysis of SARS-CoV-2 human CD4 and CD8 T-cell epitope data compiled from these studies was also reported, identifying 1400 different reported SARS-CoV-2 epitopes and revealing discrete immunodominant regions of the virus and epitopes that are more prevalently recognized. This remarkable breadth of epitope repertoire has implications for vaccine design, cross-reactivity and for immune escape by SARS-CoV-2 variants.

Reference

[https://www.cell.com/cell-host-microbe/fulltext/S1931-3128\(21\)00238-9](https://www.cell.com/cell-host-microbe/fulltext/S1931-3128(21)00238-9)

Publication Date: May 20, 2021

Structural and functional ramifications of antigenic drift in recent SARS-CoV-2 variants

Abstract

Neutralizing antibodies (nAbs) elicited against the receptor-binding site (RBS) of the spike protein of wild-type SARS-CoV-2 are generally less effective against recent variants of concern. RBS residues E484, K417 and N501 are mutated in variants first described in South Africa (B.1.351) and Brazil (P.1). We analyzed their effects on ACE2 binding and K417N and E484K mutations on nAbs isolated from COVID-19 patients. Binding and neutralization of the two most frequently elicited antibody families (IGHV3-53/3-66 and IGHV1-2), which can both bind the RBS in alternate binding modes, are abrogated by K417N, E484K, or both. These effects can be structurally explained by their extensive interactions with RBS nAbs. However, nAbs to the more conserved, cross-neutralizing CR3022 and S309 sites were largely unaffected. The results have implications for next-generation vaccines and antibody therapies.

Reference

<https://science.sciencemag.org/content/early/2021/05/19/science.abh1139>

Mass SARS-CoV-2 serological screening, a population-based study in the Principality of Andorra

Abstract

Background: Andorra is a small country located in the Pyrenees attracting millions of visitors for tourism, mostly associated with skiing, and nature-related activities. As its neighbouring countries, Spain and France, it has been heavily affected by the COVID-19 pandemic. We estimated SARS-CoV-2 seroprevalence in the entire country by universal serological testing under a lockdown environment.

Methods: A total of 77,543 inhabitants of Andorra were invited to participate in the study. From 4-28 May, 2020, two cross sectional serological surveys were conducted using a rapid serological test (nCOV IgG/IgM) on a finger prick blood sample in 59 drive-through or walk-through checkpoints, all over Andorra. We calculated seroprevalence of antibodies against SARS-CoV-2 and analysed the main sociodemographic factors associated with being seropositive.

Findings: 70,494 inhabitants (90.9% of the population) participated in at least one survey. Overall seroprevalence was 11.0%. The most affected age groups were those over 90 years old (15.2%) and 80-89 (13.8%), followed by adults 50-59 (13.6%) and adolescents 10-19 (13.7%). Most seropositive participants, 6,061 (95.1%), were asymptomatic before the surveys. The multivariable analysis showed that the odds of being seropositive was higher among seasonal workers (OR 2.41; 95% CI 1.07-5.45) or in the population living in La Massana region, a popular ski-related area (OR 2.66; 95% CI 2.44-2.89). A higher seroprevalence was observed in those familiar nuclei with greater numbers of cohabitants: 18% in families with 6 household members or more; 13% in medium size families (3/4/5 people) and 12% in small size (1 to 2 people) nuclei.

Interpretation: The prevalence of antibodies against SARS-CoV-2 in the population of Andorra was high during the first wave of the pandemic. Seasonal workers and inhabitants based in La Massana presented a higher seroprevalence. Mass antibody screening allows to identify infection hotspots and should contribute to the design of tailored interventions to prevent SARS-CoV-2 transmission in Andorra.

Reference

[https://www.thelancet.com/journals/lanepi/article/PIIS2666-7762\(21\)00096-X/fulltext](https://www.thelancet.com/journals/lanepi/article/PIIS2666-7762(21)00096-X/fulltext)

Structural and functional ramifications of antigenic drift in recent SARS-CoV-2 variants

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ACE2 binding and K417N and E484K mutations on nAbs isolated from COVID-19 patients. Binding and neutralization of the two most frequently elicited antibody families (IGHV3-53/3-66 and IGHV1-2), which can both bind the RBS in alternate binding modes, are abrogated by K417N, E484K, or both. These effects can be structurally explained by their extensive interactions with RBS nAbs. However, nAbs to the more conserved, cross-neutralizing CR3022 and S309 sites were largely unaffected. The results have implications for next-generation vaccines and antibody therapies.

Reference

<https://science.sciencemag.org/content/early/2021/05/19/science.abh1139>

Impact of daily high dose oral vitamin D therapy on the inflammatory markers in patients with COVID 19 disease

Abstract

COVID 19 is known to cause immune dysregulation and vitamin D is a known immunomodulator. This study aims to objectively investigate the impact of Pulse D therapy in reducing the inflammatory markers of COVID-19. Consented COVID-19 patients with hypovitaminosis D were evaluated for inflammatory markers (N/L ratio, CRP, LDH, IL6, Ferritin) along with vitamin D on 0th day and 9th/11th day as per their respective BMI category. Subjects were randomised into VD and NVD groups. VD group received Pulse D therapy (targeted daily supplementation of 60,000 IUs of vitamin D for 8 or 10 days depending upon their BMI) in addition to the standard treatment. NVD group received standard treatment alone. Differences in the variables between the two groups were analysed for statistical significance. Eighty seven out of one hundred and thirty subjects have completed the study (VD:44, NVD:43). Vitamin D level has increased from 16 ± 6 ng/ml to 89 ± 32 ng/ml after Pulse D therapy in VD group and highly significant ($p < 0.01$) reduction of all the measured inflammatory markers was noted. Reduction of markers in NVD group was insignificant ($p > 0.05$). The difference in the reduction of markers between the groups (NVD vs VD) was highly significant ($p < 0.01$). Therapeutic improvement in vitamin D to 80–100 ng/ml has significantly reduced the inflammatory markers associated with COVID-19 without any side effects. Hence, adjunctive Pulse D therapy can be added safely to the existing treatment protocols of COVID-19 for improved outcomes.

Reference

<https://www.nature.com/articles/s41598-021-90189-4>

Metabolomics and computational analysis of the role of monoamine oxidase activity in delirium and SARS-COV-2 infection

Abstract

Delirium is an acute change in attention and cognition occurring in ~65% of severe SARS-CoV-2 cases. It is also common following surgery and an indicator of brain vulnerability and risk for the development of dementia. In this work we analyzed the underlying role of metabolism in delirium-susceptibility in the postoperative setting using metabolomic profiling of cerebrospinal fluid and blood taken from the same patients prior to planned orthopaedic surgery. Distance correlation analysis and Random Forest (RF) feature selection were used to determine changes in metabolic networks. We found significant concentration differences in several amino acids, acylcarnitines and polyamines linking delirium-prone patients to known factors in Alzheimer's disease such as monoamine oxidase B (MAOB) protein. Subsequent computational structural comparison between MAOB and angiotensin converting enzyme 2 as well as protein-protein docking analysis showed that there potentially is strong binding of SARS-CoV-2 spike protein to MAOB. The possibility that SARS-CoV-2 influences MAOB activity leading to the observed neurological and platelet-based complications of SARS-CoV-2 infection requires further investigation.

Reference

<https://www.nature.com/articles/s41598-021-90243-1>

Sequential infection with H1N1 and SARS-CoV-2 aggravated COVID-19 pathogenesis in a mammalian model, and co-vaccination as an effective method of prevention of COVID-19 and influenza

Abstract

Influenza A virus may circulate simultaneously with the SARS-CoV-2 virus, leading to more serious respiratory diseases during this winter. However, the influence of these viruses on disease outcome when both influenza A and SARS-CoV-2 are present in the host remains unclear. Using a mammalian model, sequential infection was performed in

ferrets and in K18-hACE2 mice, with SARS-CoV-2 infection following H1N1. We found that co-infection with H1N1 and SARS-CoV-2 extended the duration of clinical manifestation of COVID-19, and enhanced pulmonary damage, but reduced viral shedding of throat swabs and viral loads in the lungs of ferrets. Moreover, mortality was increased in sequentially infected mice compared with single-infection mice. Compared with single-vaccine inoculation, co-inoculation of PiCoVacc (a SARS-CoV-2 vaccine) and the flu vaccine showed no significant differences in neutralizing antibody titers or virus-specific immune responses. Combined immunization effectively protected K18-hACE2 mice against both H1N1 and SARS-CoV-2 infection. The findings indicated the development of systematic models of co-infection of H1N1 and SARS-CoV-2, which together notably enhanced pneumonia in ferrets and mice, as well as demonstrated that simultaneous vaccination against H1N1 and SARS-CoV-2 may be an effective prevention strategy for the coming winter.

Reference

<https://www.nature.com/articles/s41392-021-00618-z>

Mass SARS-CoV-2 serological screening, a population-based study in the Principality of Andorra

Abstract

Background: Andorra is a small country located in the Pyrenees attracting millions of visitors for tourism, mostly associated with skiing, and nature-related activities. As its neighbouring countries, Spain and France, it has been heavily affected by the COVID-19 pandemic. We estimated SARS-CoV-2 seroprevalence in the entire country by universal serological testing under a lockdown environment.

Methods: A total of 77,543 inhabitants of Andorra were invited to participate in the study. From 4-28 May, 2020, two cross sectional serological surveys were conducted using a rapid serological test (nCOV IgG/IgM) on a finger prick blood sample in 59 drive-through or walk-through checkpoints, all over Andorra. Seroprevalence of antibodies were calculated against SARS-CoV-2 and analysed the main sociodemographic factors associated with being seropositive.

Findings: 70,494 Inhabitants (90.9% of the population) participated in at least one survey. Overall seroprevalence was 11.0%. The most affected age groups were those over 90 years old (15.2%) and 80-89 (13.8%), followed by adults 50-59 (13.6%) and adolescents 10-19 (13.7%). Most seropositive participants, 6,061 (95.1%), were asymptomatic before the surveys. The multivariable analysis showed that the odds of being seropositive was higher among seasonal workers (OR 2.41; 95% CI 1.07-5.45) or in the population living in La Massana region, a popular ski-related area (OR 2.66; 95% CI 2.44-2.89). A higher seroprevalence was observed in those familiar nuclei with greater numbers of cohabitants: 18% in families with 6 household members or more; 13% in medium size families (3/4/5 people) and 12% in small size (1 to 2 people) nuclei.

Interpretation: The prevalence of antibodies against SARS-CoV-2 in the population of Andorra was high during the first wave of the pandemic. Seasonal workers and inhabitants based in La Massana presented a higher seroprevalence. Mass antibody screening allows to identify infection hotspots and should contribute to the design of tailored interventions to prevent SARS-CoV-2 transmission in Andorra.

Reference

[https://www.thelancet.com/journals/lanepi/article/PIIS2666-7762\(21\)00096-X/fulltext](https://www.thelancet.com/journals/lanepi/article/PIIS2666-7762(21)00096-X/fulltext)

CORRESPONDANCE

Publication Date: May 25, 2021

SARS-CoV-2 vaccination in immunosuppressed patients with inflammatory bowel disease: Should our approach change?

Since the publication of the British Society of Gastroenterology (BSG) Inflammatory Bowel Disease (IBD) section position statement on SARS-CoV-2 vaccination, developments concerning vaccine safety have prompted the BSG to review its guidance. Concerns have arisen with the well-publicised association between the ChAdOx1 nCoV-19 (Oxford/AstraZeneca) vaccine and very rare reports of serious thromboembolic events, including cerebral venous sinus thrombosis, with concurrent thrombocytopenia. There have been similar reports with the JNJ-78436735 (Johnson & Johnson) vaccine in the USA. This news will be of particular interest to patients with IBD, who are at increased risk of venous thromboembolism, especially during active disease. For more details, read the link given below.

Reference

[https://www.thelancet.com/journals/langas/article/PIIS2468-1253\(21\)00184-9/fulltext](https://www.thelancet.com/journals/langas/article/PIIS2468-1253(21)00184-9/fulltext)

Publication Date: May 21, 2021

Urgent needs to accelerate the race for COVID-19 therapeutics

On December 8, 2020, a 91-year-old woman made history as the first person to receive the COVID-19 vaccine in the United Kingdom. Worldwide vaccination coverage will take time, especially in low-middle-income countries (LMICs) where access to coronavirus vaccines is limited and health systems are ill equipped to deal with sustained pressures associated with COVID-19. Meanwhile, hospital and critical care capacity will remain strained and basic therapies, including oxygen, are in urgent short supply.[1]

COVID-19 has disproportionately impacted the world's poorest and most vulnerable, posing additional challenges in achieving the Sustainable Development Goals.[2] In addition to basic supportive therapies, there are still not enough effective therapeutic interventions widely available. There remains an urgent need to develop efficacious

COVID-19 therapeutics to prevent severity and mortality, and to forestall the collapse of overburdened health systems in resource-limited settings. For more details, read the link given below.

Reference

[https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370\(21\)00191-7/fulltext](https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00191-7/fulltext)

Publication Date: May 20, 2021

Psychosis and COVID-19: Is it time to pre-emptively revise advanced directives?

Historically, people with psychosis have been stripped of their right to autonomous decisions regarding their treatment. Lack of insight and impaired decision-making capacity is often cited as the justification for this authoritarian view. However, it is increasingly recognised that decision-making capacity in people with psychosis is dynamic, with intermittent periods of intactness. Worldwide, there has been growing advocacy to grant more autonomy for people with psychosis to make decisions regarding their treatment and life. An advanced directive is one such legal provision wherein people with mental illness can decide on the nature of health care they wish to receive.

If the COVID-19 pandemic has affected the very fabric of everyday life, then can an advanced directive made before the pandemic genuinely serve its intended purpose? In this instance, a pre-commitment directive might not be the true reflection of autonomy across the continuum of time given the dynamic nature of changes. This does not mean, however, that the autonomy of the patient should be compromised. It is during these challenging times that advanced directives are to be protected with utmost sanctity. This brings us to the next challenge about how a mental health-care provider should manage this conundrum. For more details, read the link given below.

Reference

[https://www.thelancet.com/journals/lanpsy/article/PIIS2215-0366\(21\)00119-X/fulltext](https://www.thelancet.com/journals/lanpsy/article/PIIS2215-0366(21)00119-X/fulltext)

COMMENT

Publication Date: May 25, 2021

A lethal mouse model using a mouse-adapted SARS-CoV-2 strain with enhanced binding to mouse ACE2 as an important platform for COVID-19 research

New SARS-CoV-2 variants continue to emerge as the COVID-19 pandemic expands. Some of these variants are considered to be “*variants of concerns*” as they may be associated with enhanced transmission, pathogenicity, and/or immune evasion. In the presented study, Huang *et al.* characterized the adaptive mutations of the mouse-adapted WBP-1 strain and identified Q493K and Q498H in the SARS-CoV-2 spike receptor-binding domain as two key mutations associated with enhanced binding affinity towards mACE2. These results are particularly relevant to the control of the ongoing COVID-19 pandemic because the presence of these and other mutations that may facilitate binding with the ACE2 of mice and/or other animal species in clinical SARS-CoV-2 variants may suggest the need for tightened source control in order to minimize the contacts between humans and these potentially infected animal species leading to interspecies transmission. For more details, read the given link below.

Reference

[https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964\(21\)00199-7/fulltext](https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(21)00199-7/fulltext)

Biomarkers for severe COVID-19

The Coronavirus Disease 2019 (COVID-19) has a wide spectrum of clinical severity. Studies have estimated that while 30–60% of COVID-19 cases are asymptomatic or mildly symptomatic, 5% of symptomatic cases are critically ill. Severe COVID-19 is usually characterized by respiratory compromise and multiorgan failure. Clinical or demographic risk factors for severe disease include older age, male sex, and chronic health conditions, especially diabetes mellitus, cardiovascular disease, immunosuppression and obesity. Genetic variations in the immune pathways or autoantibodies against type I interferon, are associated with severe COVID-19.

Host response to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection can be beneficial or deleterious, and plays an important role in the

pathogenesis of COVID-19. For example, a rare Kawasaki-like multisystem inflammatory syndrome in children (also known as paediatric inflammatory multisystem syndrome) is believed to be caused by an improper autoimmune response. But unlike other severe respiratory virus infections, severe SARS-CoV-2 infection invokes a more limited inflammatory response, wherein cytokine storm is not a major feature. To identify host factors or pathways that are associated with poor outcome, van de Beek et al. analysed the changes of 64 blood biomarkers that are related to endothelial activation, inflammation, neutrophil activation and neutrophil extracellular traps (NET) formation, activation of the complement, coagulopathy and epithelial barrier disruption. As reported in this issue of EBioMedicine, they compared the expression profiles of these factors in two cohorts of COVID-19 patients. The first cohort included patients admitted to the general ward, and the outcome measure was admission to intensive care unit (ICU) or mortality. The second cohort included patients admitted to the ICU, and the outcome measure was 12-week mortality. While some factors/pathways were common to both cohorts, there were several factors that demonstrated characteristic changes unique to either the general ward or ICU cohort. The strongest predictors for poor outcome in the general ward were endothelial activation and chemotaxis. On the other hand, the markers of poor prognosis in the ICU included those involved in enhanced inflammation, activation of complement system and coagulation. The authors concluded that interventions in the general ward should focus on strategies that enhance endothelial integrity and limit chemotaxis, while ICU patients require interventions on multiple pathways.

The unique feature of the study by van de Beek et al., as compared with other studies on host response of COVID-19 patients, is the determination of deleterious markers in two distinct cohorts with different clinical severity. The biological insights of the immune response based on the patients' clinical severity are especially relevant for clinicians, as previous studies showed that the efficacy of treatment is associated with disease severity. For example, dexamethasone is most efficacious among patients requiring oxygen supplementation but not among those with mild disease. On the other hand, the monoclonal antibody LY-CoV555 was only efficacious among out-patients but not hospitalized patients. Hence, instead of a one-size-fits-all approach, clinicians should treat their patients according to the different stages of patients' illness.

Endothelial dysfunction is of particular concern in COVID-19, which can be caused by direct endothelial cell infection by SARS-CoV-2, or by the immune response towards SARS-CoV-2. Endotheliitis can trigger the innate immune response, and can contribute to thromboembolism and multisystem involvement of COVID-19. The prevalence of alveolar capillary microthrombi was found to be 9 times higher for patients with COVID-19 than those with influenza. In this study, a heightened endothelial activation among more severe patients in the general ward suggested that the endothelial dysfunction occurs early in the disease course, even before the development of clinical deterioration. Therefore, early intervention that ameliorates endothelial dysfunction can theoretically prevent the progression of COVID-19. Several such interventions, such as defibrotide and heparanase inhibitors, have been proposed.

The study by van de Beek et al. can help researchers in finding potential host-directed treatment targets. However, it should be noted that inhibitors against these biomarkers or pathways may or may not be clinically useful. For example, interleukin 6 (IL-6) was found to be a biomarker for unfavourable outcome in both general ward and ICU cohorts. However, there are conflicting data regarding the use of IL-6 receptor antagonist in COVID-19 patients, including several well-conducted randomized clinical trials. While the REMAP-CAP Investigators showed that IL-6 receptor antagonists improved the survival of critically ill COVID-19 patients, Salama et al. did not find any survival benefit for IL-6 receptor antagonists. Hence, these inhibitors must be evaluated carefully in animal studies and clinical trials. Furthermore, as multiple pathways lead to unfavourable outcome, a combination of these host factor inhibitors may provide additive or synergistic benefit. For more details, read the given link below.

Reference

[https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964\(21\)00198-5/fulltext](https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(21)00198-5/fulltext)

REPORT

Publication Date: May 26, 2021

Intrinsic signal amplification by type-III CRISPR-Cas systems provides a sequence-specific SARS-CoV-2 diagnostic

There is an urgent need for inexpensive new technologies that enable fast, reliable, and scalable detection of viruses. Here we repurposed the type III CRISPR-Cas system for sensitive and sequence specific detection of SARS-CoV-2. RNA recognition by the type III CRISPR complex triggers Cas10-mediated polymerase activity, which simultaneously generates pyrophosphates, protons and cyclic oligonucleotides. It was shown that all three Cas10-polymerase products are detectable using colorimetric or fluorometric readouts. We design 10 guide RNAs that target conserved regions of SARS-CoV-2 genomes. Multiplexing improves the sensitivity of amplification-free RNA detection from 107 copies/ μ L for a single guide RNA, to 106 copies/ μ L for 10 guides. To decrease the limit of detection to levels that are clinically relevant, we developed a two-pot reaction consisting of RT-LAMP followed by T7-transcription and type III CRISPR-based detection. The two-pot reaction has a sensitivity of 200 copies/ μ l and is completed using patient samples in less than 30 minutes.

Reference

[https://www.cell.com/cell-reports-medicine/fulltext/S2666-3791\(21\)00162-2](https://www.cell.com/cell-reports-medicine/fulltext/S2666-3791(21)00162-2)

Publication Date: May 21, 2021

Landscape of epitopes targeted by T cells in 852 convalescent COVID-19 patients: Meta-analysis, immunoprevalence and web platform

Knowledge of the epitopes of SARS-CoV-2 targeted by T cells in convalescent patients is important for understanding T cell immunity against COVID-19. This information can aid the development and assessment of COVID-19 vaccines, and inform novel diagnostic technologies. Here a unified description was provided and meta-analysis of SARS-CoV-2 T cell epitopes compiled from 18 studies of cohorts of convalescent COVID-19 patients (852 patients in total). The analysis demonstrates the broad diversity

of T cell epitopes that have been recorded for SARS-CoV-2. A large majority are seemingly unaffected by current variants of concern. A set of 20 immunoprevalent epitopes was identified that induced T cell responses in multiple cohorts and in a large fraction of tested patients. The landscape of SARS-CoV-2 T cell epitopes that we describe can help guide immunological studies, including those related to vaccines and diagnostics. A web-based platform has been developed to help complement these efforts.

Reference

[https://www.cell.com/cell-reports-medicine/fulltext/S2666-3791\(21\)00155-5](https://www.cell.com/cell-reports-medicine/fulltext/S2666-3791(21)00155-5)

Cross-reactive coronavirus antibodies with diverse epitope specificities and Fc effector functions

Abstract

The continual emergence of novel coronavirus (CoV) strains, like SARS-CoV-2, highlights the critical need for broadly reactive therapeutics and vaccines against this family of viruses. From a recovered SARS-CoV donor sample, we identify and characterize a panel of six monoclonal antibodies that cross-react with CoV spike (S) proteins from the highly pathogenic SARS-CoV and SARS-CoV-2, and demonstrate a spectrum of reactivity against other CoV. Epitope mapping reveals that these antibodies recognize multiple epitopes on SARS-CoV-2 S, including the receptor binding domain, N-terminal domain, and S2 subunit. Functional characterization demonstrates that the antibodies mediate phagocytosis - and in some cases trogocytosis - but not neutralization in vitro. When tested in vivo in murine models, two of the antibodies demonstrate a reduction in hemorrhagic pathology in the lungs. The identification of cross-reactive epitopes recognized by functional antibodies expands the repertoire of targets for pan-coronavirus vaccine design strategies.

Reference

[https://www.cell.com/cell-reports-medicine/fulltext/S2666-3791\(21\)00156-7](https://www.cell.com/cell-reports-medicine/fulltext/S2666-3791(21)00156-7)

Face masks effectively limit the probability of SARS-CoV-2 transmission

Abstract

Airborne transmission by droplets and aerosols is important for the spread of viruses. Face masks are a well-established preventive measure, but their effectiveness for mitigating SARS-CoV-2 transmission is still under debate. It was shown that variations in mask efficacy can be explained by different regimes of virus abundance and related to population-average infection probability and reproduction number. For SARS-CoV-2, the viral load of infectious individuals can vary by orders of magnitude. It was found that most environments and contacts are under conditions of low virus abundance (virus-limited) where surgical masks are effective at preventing virus spread. More advanced masks and other protective equipment are required in potentially virus-rich indoor environments including medical centers and hospitals. Masks are particularly effective in combination with other preventive measures like ventilation and distancing.

Reference

<https://science.sciencemag.org/content/early/2021/05/19/science.abg6296>

SARS-CoV-2 infection induces beta cell transdifferentiation

Recent clinical data has suggested a correlation between Coronavirus disease 19 (COVID-19) and diabetes. Here, we describe the detection of SARS-CoV-2 viral antigen in pancreatic beta cells in autopsy samples from individuals with COVID-19. Single-cell RNA-sequencing and immunostaining from ex vivo infections confirmed that multiple types of pancreatic islet cells were susceptible to SARS-CoV-2, eliciting a cellular stress response and the induction of chemokines. Upon SARS-CoV-2 infection, beta cells showed a lower expression of insulin and a higher expression of alpha and acinar cell markers, including glucagon and trypsin1, respectively, suggesting cellular transdifferentiation. Trajectory analysis indicated that SARS-CoV-2 induced eIF2 pathway-mediated beta cell transdifferentiation, a phenotype that could be reversed with trans-integrated stress response inhibitor (trans-ISRIB). Altogether, this study

demonstrates an example of SARS-CoV-2 infection causing cell fate change, which provides further insight into the pathomechanisms of COVID-19.

Reference

[https://www.cell.com/cell-metabolism/fulltext/S1550-4131\(21\)00232-1](https://www.cell.com/cell-metabolism/fulltext/S1550-4131(21)00232-1)

Direct derivation of human alveolospheres for SARS-CoV-2 infection modeling and drug screening

Although the main cellular target of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is thought to be alveolar cells, the absence of their tractable culture system has precluded the development of a clinically-relevant SARS-CoV-2 infection model. Here, an efficient human alveolosphere culture method and sphere-based drug testing platform were established for SARS-CoV-2. Alveolospheres exhibited indolent growth in a Wnt and R-spondin dependent manner. Gene expression, immunofluorescence and electron microscopy analyses revealed the presence of alveolar cells in alveolospheres. Alveolospheres expressed ACE2 and allowed SARS-CoV-2 to propagate nearly 100,000- fold in three days of infection. While lopinavir and nelfinavir, protease inhibitors used for the treatment of HIV infection, had a modest anti-viral effect on SARS-CoV-2, remdesivir, a nucleotide prodrug, showed anti-viral effect at the concentration comparable to the circulating drug level. These results demonstrated the validity of alveolosphere culture system for the development of therapeutic agents to combat SARS-CoV-2.

Reference

[https://www.cell.com/cell-reports/fulltext/S2211-1247\(21\)00569-6](https://www.cell.com/cell-reports/fulltext/S2211-1247(21)00569-6)

NEWS LETTER

Publication Date: May 26, 2021

Scientists claim to have solved Covid vaccine blood-clot puzzle

Scientists in Germany claim to have cracked the cause of the rare blood clots linked to the Oxford/AstraZeneca and Johnson & Johnson (J&J) coronavirus vaccines and believe the jabs could be tweaked to stop the reaction happening altogether. Rolf Marschalek, a professor at Goethe University in Frankfurt who has been leading studies into the rare condition since March, said his research showed the problem sat with the adenovirus vectors that both vaccines use to deliver the genetic instructions for the spike protein of the SARS-COV-2 virus into the body.

The delivery mechanism means the vaccines send the DNA gene sequences of the spike protein into the cell nucleus rather than the cytosol fluid found inside the cell where the virus normally produces proteins, Marschalek and other scientists said in a preprint paper released on Wednesday.

Once inside the cell nucleus, certain parts of the spike protein DNA are spliced, or split apart, creating mutant versions, which are unable to bind to the cell membrane where important immunisation takes place. The floating mutant proteins are instead secreted by cells into the body, triggering blood clots in roughly one in 100,000 people, according to Marschalek's theory.

In contrast, mRNA-based vaccines, such as the jabs developed by BioNTech/Pfizer and Moderna, deliver the spike's genetic material to the cell fluid and it never enters the nucleus.

The rare blood-clotting reaction that has disrupted the rollout of the AstraZeneca and J&J shots has been recorded in 309 of the 33m people who have received the AstraZeneca vaccine in the UK, causing 56 deaths. In Europe, at least 142 people have experienced the blood clots out of 16m recipients of the vaccine. In response, use of the AstraZeneca jab has been restricted or suspended in more than a dozen countries. J&J began the rollout of its vaccine in Europe with a warning on its label in April after a brief delay because of the concerns. For more details, read the link given below.

Reference

<https://www.ft.com/content/f76eb802-ec05-4461-9956-b250115d0577>

HIGHLIGHTS

Publication Date: May 26, 2021

Cellular disturbances in COVID-19

Two recent studies utilizing multi-omics single-cell analyses provide new insights into potential immunopathogenesis associated with severe COVID-19. In Nature Medicine, Stephenson et al. performed gene expression analysis on peripheral blood mononuclear cells obtained from a cohort of patients with COVID-19 of varying severity. Notably, they identify a C1Q-expressing CD16+ monocyte subset associated with more severe disease. C1q+CD16+ monocytes had increased interaction with platelets, a finding that is linked with increased platelet activation and increased frequencies of mobilized megakaryocyte precursors in patients' blood. In Nature, Delorey et al. present a single-cell and spatial cell atlas of gene expression in lung samples obtained at autopsy of patients with critical COVID-19. They show severe reductions in lung AT2 epithelial cells along with reduced surfactant production and perturbations in the regeneration of AT1 epithelial cells, which ultimately lead to compromised lung function. Both studies can serve as rich dataset resources for further hypothesis-driven investigations of COVID-19-associated immunopathology.

Reference

<https://www.nature.com/articles/s41590-021-00953-x>

PERSONAL VIEW

Publication Date: May 25, 2021

SARS-CoV-2 vaccines for all but a single dose for COVID-19 survivors

There is an urgent need to develop policies that maximize the number of people who receive vaccines without sacrificing the efficacy of immune protection given that we are still in the midst of the COVID-19 pandemic with a limited supply of authorized SARS-CoV-2 vaccines. Several policy proposals have recently been discussed including delaying the second vaccine dose for everyone or focusing vaccinations in a preferred manner towards naïve individuals. We believe the best solution is to provide individuals who already had a SARS-CoV-2 infection receive only one (rather than two) shots of the currently authorized mRNA vaccines (BNT162b2/Pfizer; mRNA-1273/Moderna). Emerging real world evidence suggest that the antibody responses to the first vaccine dose in individuals with prior SARS-CoV-2 infection is equal to or exceeds the antibody titers found in naïve individuals after the second dose. Changing the current vaccine recommendation to provide only one dose of vaccine to COVID-19 survivors would free up many urgently needed vaccine doses. With the additional available vaccines, there would be no need to delay the second vaccine dose for naïve individuals.

Recent findings from several groups independently report high antibody titers and neutralization activity after the first dose of Pfizer or Moderna RNA vaccine in individuals who already had SARS-CoV-2 infections. While each of these recent studies has a limited number of participants, the overall conclusions are complementary and clear with respect to the fact that individuals with pre-existing immunity developed uniformly high antibody titers. The observed increased reactogenicity experienced after the first dose in COVID-19 survivors combined with rapid increase in antibody titers supports the notion that the first vaccine dose acts as boost for the immune responses acquired after natural infection. In such a scenario, the second vaccine dose administered within 21-30 days after the first dose results in little increase in antibody titers. It will be important to assess whether the same principles apply to vaccines developed on different platforms, with broad implications for global health.

Over 149 million people worldwide (32 million in the US) have been diagnosed with a SARS-CoV-2 infection since the beginning of the pandemic over a year ago with approximately 10% of the US population having had COVID-19 (Coronavirus COVID-19 Global Cases by Johns Hopkins CSSE, accessed 4/29/2021). Seroprevalence studies have shown pronounced geographic differences: for example in some of the US metropolitan centers that were hard hit during the first pandemic wave (e.g., NYC) around 20-25% of the inhabitants have antibodies to SARS-CoV-2. Thus, in some regions with a high percentage of confirmed previous infections, the mRNA vaccine supply could instantly increase without any significant increase in resources, freeing up doses to help contain the pandemic more swiftly, and potentially saving lives. Active antibody screening for SARS-CoV2 spike antibodies could further identify those with previous infection and increase the available supply even more.

Since the science shows that everyone benefits from the first dose of the mRNA vaccination, especially in the context of emerging variants of concern, COVID-19 survivors should not be deferred from vaccination. To the contrary, COVID-19 survivors should be offered a single dose, which would provide the needed immune boost to achieve high levels of immunity while limiting side effects and expanding the available vaccine supply to protect more individuals at risk in the immediate future. As vaccine supply chain limitations ease, booster vaccinations based on personalized schedules (informed by, for example, antibody titers) maybe required depending on the durability of the vaccine induced immune protection.

Reference

[https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964\(21\)00194-8/fulltext](https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(21)00194-8/fulltext)