

COVID-19

Aug 27- Sep 02, 2020



RESEARCH PUBLICATIONS

Publication Date: Sep 02, 2020

A comparison of four serological assays for detecting anti-SARS-CoV-2 antibodies in human serum samples from different populations

Abstract

It is of paramount importance to evaluate the prevalence of both asymptomatic and symptomatic cases of SARS-CoV-2 infection and their differing antibody response profiles. Here, we performed a pilot study of four serological assays to assess the amounts of anti-SARS-CoV-2 antibodies in serum samples obtained from 491 healthy individuals before the SARS-CoV-2 pandemic, 51 individuals hospitalized with COVID-19, 209 suspected cases of COVID-19 with mild symptoms, and 200 healthy blood donors. We used two ELISA assays that recognized the full-length nucleoprotein (N) or trimeric spike (S) protein ectodomain of SARS-CoV-2. In addition, we developed the S-Flow assay that recognized the S protein expressed at the cell surface using flow cytometry, and the luciferase immunoprecipitation system (LIPS) assay that recognized diverse SARS-CoV-2 antigens including the S1 domain and the carboxyl-terminal domain of N by immunoprecipitation. We obtained similar results with the four serological assays. Differences in sensitivity were attributed to the technique and the antigen used. High anti-SARS-CoV-2 antibody titers were associated with neutralization activity, which was assessed using infectious SARS-CoV-2 or lentiviral-S pseudotype virus. In hospitalized patients with COVID-19, seroconversion and virus neutralization occurred between 5 and 14 days after symptom onset, confirming previous studies. Seropositivity was detected in 32% of mildly symptomatic individuals within 15 days of symptom onset and in 3% of healthy blood donors. The four antibody assays that we

used enabled a broad evaluation of SARS-CoV-2 seroprevalence and antibody profiling in different subpopulations within one region.

Reference

<https://stm.sciencemag.org/content/12/559/eabc3103>

Disease severity dictates SARS-CoV-2-specific neutralizing antibody responses in COVID-19

Abstract

COVID-19 patients exhibit differential disease severity after SARS-CoV-2 infection. It is currently unknown as to the correlation between the magnitude of neutralizing antibody (NAb) responses and the disease severity in COVID-19 patients. In a cohort of 59 recovered patients with disease severity including severe, moderate, mild, and asymptomatic, we observed the positive correlation between serum neutralizing capacity and disease severity, in particular, the highest NAb capacity in sera from the patients with severe disease, while a lack of ability of asymptomatic patients to mount competent NAb. Furthermore, the compositions of NAb subtypes were also different between recovered patients with severe symptoms and with mild-to-moderate symptoms. These results reveal the tremendous heterogeneity of SARS-CoV-2-specific NAb responses and their correlations to disease severity, highlighting the needs of future vaccination in COVID-19 patients recovered from asymptomatic or mild illness.

Reference

<https://www.nature.com/articles/s41392-020-00301-9>

Development and initial psychometric properties of a panic buying scale during COVID-19 pandemic

Abstract

Fear is a powerful driver of human behavior, even more during times of crisis. Panic buying occurs when fear and panic influence behavior leading people to buy more things than usual. So far, no specific scale on this has been found in the major

databases, thus the aim of this exploratory study is to develop a Panic Buying Scale (PBS) during COVID-19 pandemic. 393 Brazilians took part in this study (251 women and 142 men), answering a sociodemographic questionnaire and instruments of these variables: (1) panic buying, (2) impulse buying, (3) temporal focus, (4) optimism, (5) risk perception, and (6) need for cognition. Data collection was conducted through an online questionnaire which was shared through social media networks, from April 10th to May 4th, 2020. Factorial exploratory and confirmatory analysis indicated that PBS has a unidimensional solution and showed satisfactory reliability indexes. Results revealed that men buy more by panic than women. PBS also was positively correlated with impulse buying, past and future temporal focus, and risk perception; as well as negatively correlated with optimism and age. Findings suggest that PBS is psychometrically acceptable in the Brazilian context. This new instrument can be useful to understand the psychosocial phenomena associated with consumer behavior. Future investigations could provide more evidences of validity in other contexts.

Reference

[https://www.cell.com/heliyon/fulltext/S2405-8440\(20\)31589-9](https://www.cell.com/heliyon/fulltext/S2405-8440(20)31589-9)

Low-cost measurement of face mask efficacy for filtering expelled droplets during speech

Abstract

Mandates for mask use in public during the recent coronavirus disease 2019 (COVID-19) pandemic, worsened by global shortage of commercial supplies, have led to widespread use of homemade masks and mask alternatives. It is assumed that wearing such masks reduces the likelihood for an infected person to spread the disease, but many of these mask designs have not been tested in practice. A simple optical measurement method was demonstrated to evaluate the efficacy of masks to reduce the transmission of respiratory droplets during regular speech. In proof-of-principle studies, a variety of commonly available mask types were compared and was observed that some mask types approach the performance of standard surgical masks, while some mask alternatives, such as neck gaiters or bandanas, offer very little protection. This measurement setup is inexpensive and can be built and operated by nonexperts,

allowing for rapid evaluation of mask performance during speech, sneezing, or coughing.

Reference

<https://advances.sciencemag.org/content/6/36/eabd3083>

Publication Date: Aug 31, 2020

Activate: Randomized clinical trial of BCG vaccination against infection in the elderly

Abstract

BCG vaccination in children protects against heterologous infections and improves survival independently of tuberculosis prevention. The phase III ACTIVATE trial assessed whether BCG has similar effects in the elderly. In this double-blind, randomized trial, elderly patients (n=198) received BCG or placebo vaccine at hospital discharge, and were followed for 12 months for new infections. At interim analysis, BCG vaccination significantly increased the time to first infection (median 16 weeks compared to 11 weeks after placebo). The incidence of new infections was 42.3% (95% CIs 31.9-53.4%) after placebo vaccination and 25.0% (95% CIs 16.4-36.16%) after BCG vaccination; most of the protection was against respiratory tract infections of probable viral origin (hazard ratio 0.21, p: 0.013). No difference in the frequency of adverse effects was found. Data show that BCG vaccination is safe and can protect the elderly against infections. Larger studies are needed to assess protection against respiratory infections, including COVID-19.

Reference

[https://www.cell.com/cell/fulltext/S0092-8674\(20\)31139-9](https://www.cell.com/cell/fulltext/S0092-8674(20)31139-9)

Integrate structural analysis, isoform diversity, and interferon-inductive propensity of ACE2 to predict SARS-CoV2 susceptibility in vertebrates

Abstract

The current new coronavirus disease (COVID-19) has caused globally near 0.4/6 million confirmed deaths/infected cases across more than 200 countries. As the etiological coronavirus (a.k.a. SARS-CoV2) may putatively have a bat origin, our understanding about its intermediate reservoir between bats and humans, especially its tropism in wild and domestic animals are mostly unknown. This constitutes major concerns in public health for the current pandemics and potential zoonosis. Previous reports using structural analysis of the viral spike protein (S) binding its cell receptor of angiotensin-converting enzyme 2 (ACE2), indicate a broad potential of SARS-CoV2 susceptibility in wild and particularly domestic animals. Through integration of key immunogenetic factors, including the existence of S-binding-void ACE2 isoforms and the disparity of ACE2 expression upon early innate immune response, we further refine the SARS-CoV2 susceptibility prediction to fit recent experimental validation. In addition to showing a broad susceptibility potential across mammalian species based on structural analysis, our results also reveal that domestic animals including dogs, pigs, cattle and goats may evolve ACE2-related immunogenetic diversity to restrict SARS-CoV2 infections. Thus, we propose that domestic animals may be unlikely to play a role as amplifying hosts unless the virus has further species-specific adaptation. Findings may relieve relevant public concerns regarding COVID-19-like risk in domestic animals, highlight virus-host coevolution, and evoke disease intervention through targeting ACE2 molecular diversity and interferon optimization.

Reference

Sang, Eric R., Yun Tian, Yuanying Gong, Laura C. Miller, and Yongming Sang. "Integrate Structural Analysis, Isoform Diversity, and Interferon-Inductive Propensity of ACE2 to Refine SARS-CoV2 Susceptibility Prediction in Vertebrates." *bioRxiv* (2020).

Robust T cell response towards spike, membrane, and nucleocapsid SARS-CoV-2 proteins is not associated with recovery in critical COVID-19 patients

Abstract

T cell immunity towards SARS-CoV-2 spike (S), membrane (M), and nucleocapsid (N)-proteins might define COVID-19 severity. Therefore, the SARS-CoV-2-reactive T cell responses were compared in moderate, severe, and critical COVID-19 patients and unexposed donors. Overlapping peptide pools of all three proteins induce SARS-CoV-2-reactive T cell response with dominance of CD4+ over CD8+ T cells and demonstrate interindividual immunity against the three proteins. M-protein induces the highest frequencies of CD4+ T cells, suggesting its relevance for diagnosis and vaccination. Importantly, T cell response of critical COVID-19 patients is robust and comparable or even superior to non-critical patients. Virus clearance and COVID-19 survival are not associated with either SARS-CoV-2 T cell kinetics or magnitude of T cell responses, respectively. Thus, this data disprove the hypothesis of insufficient SARS-CoV-2-reactive immunity in critical COVID-19. Conversely, it indicates that activation of differentiated memory effector T cells could cause hyper-reactivity and immunopathogenesis in critical patients.

Reference

Thieme, Constantin J., Moritz Anft, Krystallenia Paniskaki, Arturo Blazquez-Navarro, Adrian Doevelaar, Felix S. Seibert, Bodo Hoelzer et al. "Robust T cell response towards spike, membrane, and nucleocapsid SARS-CoV-2 proteins is not associated with recovery in critical COVID-19 patients." *Cell Reports Medicine* (2020): 100092 (I.F.: 8.109).

Genetics and COVID-19: How to protect the susceptible

Abstract

Along with the potential for breakthroughs in care and prevention, the search for genetic mechanisms underlying the spread and severity of COVID-19 introduces the risk of

discrimination against those found to have markers for susceptibility. New legal protections were proposed to mitigate gaps in protections under existing laws.

Reference

Field, Robert I., Anthony W. Orlando, and Arnold J. Rosoff. "Genetics and COVID-19: How to Protect the Susceptible." *Trends in Genetics* (2020) (I.F.: 11.333).

Publication Date: Aug 28, 2020

Outcomes following SARS-CoV-2 infection in liver transplant recipients: An international registry study

Abstract

Background: Despite concerns that patients with liver transplants might be at increased risk of adverse outcomes from COVID-19 because of coexisting comorbidities and use of immunosuppressants, the effect of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection on this patient group remains unclear. We aimed to assess the clinical outcomes in these patients.

Methods: In this multicentre cohort study, data was collected on patients with laboratory-confirmed SARS-CoV-2 infection, who were older than 18 years, who had previously received a liver transplant, and for whom data had been submitted by clinicians to one of two international registries (COVID-Hep and SECURE-Cirrhosis) at the end of the patient's disease course. Patients without a known hospitalisation status or mortality outcome were excluded. For comparison, data from a contemporaneous cohort of consecutive patients with SARS-CoV-2 infection who had not received a liver transplant were collected from the electronic patient records of the Oxford University Hospitals National Health Service Foundation Trust. We compared the cohorts with regard to several outcomes (including death, hospitalisation, intensive care unit [ICU] admission, requirement for intensive care, and need for invasive ventilation). A propensity score-matched analysis was done to test for an association between liver transplant and death.

Findings: Between March 25 and June 26, 2020, data were collected for 151 adult liver transplant recipients from 18 countries (median age 60 years [IQR 47–66], 102 [68%] men, 49 [32%] women) and 627 patients who had not undergone liver transplantation (median age 73 years [44–84], 329 [52%] men, 298 [48%] women). The groups did not differ with regard to the proportion of patients hospitalised (124 [82%] patients in the liver transplant cohort vs 474 [76%] in the comparison cohort, $p=0.106$), or who required intensive care (47 [31%] vs 185 [30%], $p=0.837$). However, ICU admission (43 [28%] vs 52 [8%], $p<0.0001$) and invasive ventilation (30 [20%] vs 32 [5%], $p<0.0001$) were more frequent in the liver transplant cohort. 28 (19%) patients in the liver transplant cohort died, compared with 167 (27%) in the comparison cohort ($p=0.046$). In the propensity score-matched analysis (adjusting for age, sex, creatinine concentration, obesity, hypertension, diabetes, and ethnicity), liver transplantation did not significantly increase the risk of death in patients with SARS-CoV-2 infection (absolute risk difference 1.4% [95% CI -7.7 to 10.4]). Multivariable logistic regression analysis showed that age (odds ratio 1.06 [95% CI 1.01 to 1.11] per 1 year increase), serum creatinine concentration (1.57 [1.05 to 2.36] per 1 mg/dL increase), and non-liver cancer (18.30 [1.96 to 170.75]) were associated with death among liver transplant recipients.

Interpretation: Liver transplantation was not independently associated with death, whereas increased age and presence of comorbidities were. Factors other than transplantation should be preferentially considered in relation to physical distancing and provision of medical care for patients with liver transplants during the COVID-19 pandemic.

Reference

Webb, Gwilym J., Thomas Marjot, Jonathan A. Cook, Costica Aloman, Matthew J. Armstrong, Erica J. Brenner, Maria-Andreea Catana et al. "Outcomes following SARS-CoV-2 infection in liver transplant recipients: an international registry study." *The Lancet Gastroenterology & Hepatology* (2020) (I.F.: 14.789).

Pathophysiology of COVID-19-associated acute respiratory distress syndrome: A multicentre prospective observational study

Abstract

Background: Patients with COVID-19 can develop acute respiratory distress syndrome (ARDS), which is associated with high mortality. The aim of this study was to examine the functional and morphological features of COVID-19-associated ARDS and to compare these with the characteristics of ARDS unrelated to COVID-19.

Methods: This prospective observational study was done at seven hospitals in Italy. We enrolled consecutive, mechanically ventilated patients with laboratory-confirmed COVID-19 and who met Berlin criteria for ARDS, who were admitted to the intensive care unit (ICU) between March 9 and March 22, 2020. All patients were sedated, paralysed, and ventilated in volume-control mode with standard ICU ventilators. Static respiratory system compliance, the ratio of partial pressure of arterial oxygen to fractional concentration of oxygen in inspired air, ventilatory ratio (a surrogate of dead space), and D-dimer concentrations were measured within 24 h of ICU admission. Lung CT scans and CT angiograms were done when clinically indicated. A dataset for ARDS unrelated to COVID-19 was created from previous ARDS studies. Survival to day 28 was assessed.

Findings: Between March 9 and March 22, 2020, 301 patients with COVID-19 met the Berlin criteria for ARDS at participating hospitals. Median static compliance was 41 mL/cm H₂O (33–52), which was 28% higher than in the cohort of patients with ARDS unrelated to COVID-19 (32 mL/cm H₂O [25–43]; $p < 0.0001$). 17 (6%) of 297 patients with COVID-19-associated ARDS had compliances greater than the 95th percentile of the classical ARDS cohort. Total lung weight did not differ between the two cohorts. CT pulmonary angiograms (obtained in 23 [8%] patients with COVID-19-related ARDS) showed that 15 (94%) of 16 patients with D-dimer concentrations greater than the median had bilateral areas of hypoperfusion, consistent with thromboembolic disease. Patients with D-dimer concentrations equal to or less than the median had ventilatory ratios lower than those of patients with D-dimer concentrations greater than the median

(1.66 [1.32–1.95] vs 1.90 [1.50–2.33]; $p=0.0001$). Patients with static compliance equal to or less than the median and D-dimer concentrations greater than the median had markedly increased 28-day mortality compared with other patient subgroups (40 [56%] of 71 with high D-dimers and low compliance vs 18 [27%] of 67 with low D-dimers and high compliance, 13 [22%] of 60 with low D-dimers and low compliance, and 22 [35%] of 63 with high D-dimers and high compliance, all $p=0.0001$).

Interpretation: Patients with COVID-19-associated ARDS have a form of injury that, in many aspects, is similar to that of those with ARDS unrelated to COVID-19. Notably, patients with COVID-19-related ARDS who have a reduction in respiratory system compliance together with increased D-dimer concentrations have high mortality rates.

Reference

Grasselli, Giacomo, Tommaso Tonetti, Alessandro Protti, Thomas Langer, Massimo Girardis, Giacomo Bellani, John Laffey *et al.* "Pathophysiology of COVID-19-associated acute respiratory distress syndrome: A multicentre prospective observational study." *The Lancet Respiratory Medicine* (2020) (I.F.: 25.094).

Human umbilical cord-derived mesenchymal stem cell therapy in patients with COVID-19: A phase 1 clinical trial

Abstract

No effective drug treatments are available for coronavirus disease 2019 (COVID-19). Host-directed therapies targeting the underlying aberrant immune responses leading to pulmonary tissue damage, death, or long-term functional disability in survivors require clinical evaluation. A parallel assigned controlled, non-randomized, phase 1 clinical trial was performed to evaluate the safety of human umbilical cord-derived mesenchymal stem cells (UC-MSCs) infusions in the treatment of patients with moderate and severe COVID-19 pulmonary disease. The study enrolled 18 hospitalized patients with COVID-19 ($n=9$ for each group). The treatment group received three cycles of intravenous infusion of UC-MSCs (3×10^7 cells per infusion) on days 0, 3, and 6. Both groups received standard COVID-treatment regimens. Adverse events, duration of clinical symptoms, laboratory parameters, length of hospitalization, serial chest computed tomography (CT) images, the PaO₂/FiO₂ ratio, dynamics of cytokines, and IgG and IgM

anti-SARS-CoV-2 antibodies were analyzed. No serious UC-MSCs infusion-associated adverse events were observed. Two patients receiving UC-MSCs developed transient facial flushing and fever, and one patient developed transient hypoxia at 12 h post UC-MSCs transfusion. Mechanical ventilation was required in one patient in the treatment group compared with four in the control group. All patients recovered and were discharged. Our data show that intravenous UC-MSCs infusion in patients with moderate and severe COVID-19 is safe and well tolerated. Phase 2/3 randomized, controlled, double-blinded trials with long-term follow-up are needed to evaluate the therapeutic use of UC-MSCs to reduce deaths and improve long-term treatment outcomes in patients with serious COVID-19.

Reference

Meng, Fanping, Ruonan Xu, Siyu Wang, Zhe Xu, Chao Zhang, Yuanyuan Li, Tao Yang *et al.* "Human umbilical cord-derived mesenchymal stem cell therapy in patients with COVID-19: A phase 1 clinical trial." *Signal Transduction and Targeted Therapy* 5, no. 1 (2020): 1-7 (I.F.: 13.493).

Prevalence of phenotypes of acute respiratory distress syndrome in critically ill patients with COVID-19: A prospective observational study

Abstract

Background: In acute respiratory distress syndrome (ARDS) unrelated to COVID-19, two phenotypes, based on the severity of systemic inflammation (hyperinflammatory and hypoinflammatory), have been described. The hyperinflammatory phenotype is known to be associated with increased multiorgan failure and mortality. In this study, we aimed to identify these phenotypes in COVID-19-related ARDS.

Methods: In this prospective observational study done at two UK intensive care units, we recruited patients with ARDS due to COVID-19. Demographic, clinical, and laboratory data were collected at baseline. Plasma samples were analysed for interleukin-6 (IL-6) and soluble tumour necrosis factor receptor superfamily member 1A (TNFR1) using a novel point-of-care assay. A parsimonious regression classifier model was used to calculate the probability for the hyperinflammatory phenotype in COVID-19 using IL-6, soluble TNFR1, and bicarbonate levels. Data from this cohort was compared

with patients with ARDS due to causes other than COVID-19 recruited to a previous UK multicentre, randomised controlled trial of simvastatin (HARP-2).

Findings: Between March 17 and April 25, 2020, 39 patients were recruited to the study. Median ratio of partial pressure of arterial oxygen to fractional concentration of oxygen in inspired air (PaO₂/FiO₂) was 18 kpa (IQR 15–21) and acute physiology and chronic health evaluation II score was 12 (10–16). 17 (44%) of 39 patients had died by day 28 of the study. Compared with survivors, patients who died were older and had lower PaO₂/FiO₂. The median probability for the hyperinflammatory phenotype was 0.03 (IQR 0.01–0.2). Depending on the probability cutoff used to assign class, the prevalence of the hyperinflammatory phenotype was between four (10%) and eight (21%) of 39, which is lower than the proportion of patients with the hyperinflammatory phenotype in HARP-2 (186 [35%] of 539). Using the Youden index cutoff (0.274) to classify phenotype, five (63%) of eight patients with the hyperinflammatory phenotype and 12 (39%) of 31 with the hypoinflammatory phenotype died. Compared with matched patients recruited to HARP-2, levels of IL-6 were similar in our cohort, whereas soluble TNFR1 was significantly lower in patients with COVID-19-associated ARDS.

Interpretation: In this exploratory analysis of 39 patients, ARDS due to COVID-19 was not associated with higher systemic inflammation and was associated with a lower prevalence of the hyperinflammatory phenotype than that observed in historical ARDS data. This finding suggests that the excess mortality observed in COVID-19-related ARDS is unlikely to be due to the upregulation of inflammatory pathways described by the parsimonious model.

Reference

Sinha, Pratik, Carolyn S. Calfee, Shiney Cherian, David Brealey, Sean Cutler, Charles King, Charlotte Killick et al. "Prevalence of phenotypes of acute respiratory distress syndrome in critically ill patients with COVID-19: A prospective observational study." *The Lancet Respiratory Medicine* (2020) (I.F.: 25.094).

Blood pressure control and adverse outcomes of COVID-19 infection in patients with concomitant hypertension in Wuhan, China

Abstract

Hypertension is a common comorbidity in hospitalized patients with COVID-19 infection. This study aimed to estimate the risks of adverse events associated with in-hospital blood pressure (BP) control and the effects of angiotensin II receptor blocker (ARB) prescription in COVID-19 patients with concomitant hypertension. In this retrospective cohort study, the anonymized medical records of COVID-19 patients were retrieved from an acute field hospital in Wuhan, China. Clinical data, drug prescriptions, and laboratory investigations were collected for individual patients with diagnosed hypertension on admission. Cox proportional hazards models were used to estimate the risks of adverse outcomes associated with BP control during the hospital stay. Of 803 hypertensive patients, 67 (8.3%) were admitted to the ICU, 30 (3.7%) had respiratory failure, 26 (3.2%) had heart failure, and 35 (4.8%) died. After adjustment for confounders, the significant predictors of heart failure were average systolic blood pressure (SBP) (hazard ratio (HR) per 10 mmHg 1.89, 95% confidence interval (CI): 1.15, 3.13) and pulse pressure (HR per 10 mmHg 2.71, 95% CI: 1.39, 5.29). The standard deviations of SBP and diastolic BP were independently associated with mortality and ICU admission. The risk estimates of poor BP control were comparable between patients receiving ARBs and those not receiving ARBs, with the only exception of a high risk of heart failure in the non-ARB group. Poor BP control was independently associated with higher risks of adverse outcomes of COVID-19. ARB drugs did not increase the risks of adverse events in hypertensive patients.

Reference

Ran, Jinjun, Ying Song, Zian Zhuang, Lefei Han, Shi Zhao, Peihua Cao, Yan Geng *et al.* "Blood pressure control and adverse outcomes of COVID-19 infection in patients with concomitant hypertension in Wuhan, China." *Hypertension Research* (2020): 1-10 (I.F.: 2.941).

NEWS LETTER

Publication Date: Sep 02, 2020

Coronavirus research updates: Antibodies persist for months rather than dwindling

Nature wades through the literature on the new coronavirus — and summarizes key papers as they appear.

Why infected primary-school pupils could be hard to spot (Sep 02, 2020):

As the new coronavirus ripped through several care homes in England, more than 80% of the residents mounted an antibody response to the virus, including 82% of those over the age of 80. During outbreaks at six residential and nursing homes, Shamez Ladhani at Public Health England in London and his colleagues tested more than 500 residents and staff for SARS-CoV-2 infection (S. N. Ladhani et al. Preprint at medRxiv <https://doi.org/d7p2>; 2020). About five weeks later, the team tested many of the same people for antibodies to SARS-CoV-2 and in particular for neutralizing antibodies, potent molecules that can block the virus from infecting cells. The team found that roughly the same proportion of staff members and care-home residents had formed antibodies to the coronavirus. And neutralizing antibodies had developed in almost 90% of both staff members and residents, including more than 80% of people over the age of 80. The authors caution that it is not clear whether antibodies against the virus guard against reinfection. The findings have not yet been peer-reviewed.

COVID-19 testing helps sleep-away summer camps to avoid outbreaks (Sep 01, 2020):

Rigorous SARS-CoV-2 testing and infection-control measures prevented outbreaks at four overnight camps in Maine that hosted hundreds of children between mid-June and mid-August.

Laura Blaisdell at the Maine Medical Center in Portland and colleagues report that the four sleep-away camps asked all attendees — both campers and staff — to be tested for SARS-CoV-2 before arrival (L. L. Blaisdell et al. *Morb. Mortal. Wkly Rep.* https://www.cdc.gov/mmwr/volumes/69/wr/mm6935e1.htm?s_cid=mm6935e1_w; 2020).

Shortly after arrival, attendees were re-tested for the virus. They were also assigned to small cohorts and spent the first 14 days of camp quarantining with members of their cohort. Of more than 1,000 attendees, 2 staff members and one camper tested positive at camp and were isolated until they tested negative. The 30 people in the camper's cohort were quarantined; all tested negative for the virus during quarantine. The authors say that the virus did not spread beyond the three infected attendees.

Why infected primary-school pupils could be hard to spot (Aug 27, 2020):

Children aged 6 to 13 are less likely to have symptoms of COVID-19 than those who are younger or older, according to a study of nearly 400 infected people under the age of 21.

Matthew Kelly and his colleagues at Duke University School of Medicine in Durham, North Carolina, studied 382 children and young adults who had had close contact with a person infected with SARS-CoV-2 (J. H. Hurst *et al.* Preprint at medRxiv <http://doi.org/d7cb>; 2020). Roughly three-quarters of the study participants tested positive for SARS-CoV-2 either before or during the study. Only 61% of infected children aged 6 to 13 showed symptoms, compared with 75% of infected study participants under age 6 and 76% of those over age 13. Children aged 6–13 who did feel ill tended to have milder symptoms than older and younger study participants. Nearly one-third of infected children with an infected sibling did not have close contact with an infected adult, implying that the virus had spread from child to child.

Reference

<https://www.nature.com/articles/d41586-020-00502-w>

WHO updates clinical care guidance with corticosteroid recommendations

On 2 September, WHO published guidance for clinicians and health care decision-makers on the use of corticosteroids in patients with COVID-19.

Corticosteroids are listed in the WHO model list of essential medicines, readily available globally at a low cost. WHO encourages countries to maintain sufficient stocks of corticosteroids to treat COVID-19 and the other disease for which they are effective,

while not maintaining excessive stocks which could deny other countries access. This guidance was developed in collaboration with the non-profit Magic Evidence Ecosystem Foundation (MAGIC), which provided methodologic support to develop and disseminate living guidance for COVID-19 drug treatments. For more details, read the link given below.

Reference

<https://www.who.int/news-room/feature-stories/detail/who-updates-clinical-care-guidance-with-corticosteroid-recommendations>

Publication Date: Sep 01, 2020

Hunting for antibodies to combat COVID-19

Antibodies produced by the body in response to infectious pathogens such as SARS-CoV-2 are at the center of the fight against COVID-19. The vaccines in development seek to train the immune system to produce neutralizing antibodies that can protect people against infection (Biopharma Dealmakers, B18, June 2020), while antibodies produced in people who have been infected with SARS-CoV-2 can be the basis for diagnostic tests, as well as starting points for the development of antibody products that could be used for prevention or treatment. In this feature, with the help of data from DealForma we look at the application of antibodies in the development of both diagnostics and treatments for the COVID-19 pandemic, with a focus on some of the partnerships established to accelerate development.

Reference

<https://www.nature.com/articles/d43747-020-01115-y>

Publication Date: Aug 28, 2020

Poop tests stop COVID-19 outbreak at University of Arizona

By testing dorm wastewater for the coronavirus, the University of Arizona may have stomped out a potential outbreak before it could spread, The Washington Post reports. Several countries and some U.S. universities have been checking sewage for RNA from

SARS-CoV-2 in people's poop, which can signal infections shortly before clinical cases and deaths appear. In Arizona, wastewater from a student dormitory contained viral RNA just days after students—who had all tested negative for COVID-19—moved into their rooms this month. The university retested all 311 residents and dorm workers and found two students who were asymptomatic but positive for the virus; they were then quarantined, officials explained in a press conference. “If we had waited until they became symptomatic and they stayed in that dorm for days, or a week, or the whole incubation period, how many other people would have been infected?” said former U.S. Surgeon General Richard Carmona, now a faculty member at the university. That suggests sewage testing “is a very good early warning system,” environmental health scientist Kevin Thomas of the University of Queensland, St. Lucia, told *The Washington Post*.

Reference

<https://www.sciencemag.org/news/2020/08/poop-tests-stop-covid-19-outbreak-university-arizona#>

Pakistan's drive to restore essential health services during COVID-19

Even in the wealthiest parts of the world, countries have been under pressure to keep their health systems well-organized and prepared to maintain essential health services for everyone as COVID-19 rages on. While Pakistan has demonstrated a strong resolve to deliver on the promise of health for all through universal health coverage (UHC), the country's health system is under immense strain from COVID-19.

Pakistan, with support from WHO, is working to strengthen basic primary health care. This will help ensure that the population receives the services they need during the pandemic, as close as possible to the communities in which they live. Ultimately, it will contribute to progress towards achieving UHC. As part of the overall WHO response to COVID-19, the UHC Partnership, along with a host of partners such as the United Nations Children's Fund (UNICEF), the United Nations Population Fund (UNFPA), the Joint United Nations Programme on HIV and AIDS (UNAIDS), World Bank and the United States Agency for International Development (USAID), have collaborated to prepare an action plan to support the Government in ensuring the continuity of essential

diagnostic, treatment and prevention services during the COVID-19 response, while protecting the safety and wellbeing of the health workforce and patients. The plan draws upon the latest WHO operational guidance for maintaining essential health services during the COVID-19 outbreak and has become a significant pillar of Pakistan's COVID-19 Preparedness and Response plan.

WHO also supported the development of the National Health Vision 2025 and provincial health sector strategies and plans. To further reach communities, WHO, through the UHC Partnership is also supporting a range of other projects such as risk communication and community engagement as part of the national response to COVID-19. For more details, read the link given below.

Reference

<https://www.who.int/news-room/feature-stories/detail/pakistan-s-drive-to-restore-essential-health-services-during-covid-19>

REPORT

Publication Date: Sep 01, 2020

Combined point of care nucleic acid and antibody testing for SARS-CoV-2 following emergence of D614G Spike Variant

Abstract

Rapid COVID-19 diagnosis in hospital is essential, though complicated by 30-50% of nose/throat swabs being negative by SARS-CoV-2 nucleic acid amplification testing (NAAT). Furthermore, the D614G spike mutant now dominates the pandemic and it is unclear how serological tests designed to detect anti-Spike antibodies perform against this variant. We assess the diagnostic accuracy of combined rapid antibody point of care (POC) and nucleic acid assays for suspected COVID-19 disease due to either wild type or the D614G spike mutant SARS-CoV-2. The overall detection rate for COVID-19 is 79.2% (95CI 57.8-92.9%) by rapid NAAT alone. Combined point of care antibody test and rapid NAAT is not impacted by D614G and results in very high sensitivity for COVID-19 diagnosis with very high specificity.

Reference

[https://www.cell.com/cell-reports-medicine/fulltext/S2666-3791\(20\)30125-7](https://www.cell.com/cell-reports-medicine/fulltext/S2666-3791(20)30125-7)

Publication Date: Aug 31, 2020

Temporal detection and phylogenetic assessment of SARS-CoV-2 in municipal wastewater

Abstract

SARS-CoV-2 has recently been detected in feces, which indicates that wastewater may be used to monitor viral prevalence in the community. Here RT-qPCR was used to monitor wastewater for SARS-CoV-2 RNA over a 74-day time course. This showed that changes in SARS-CoV-2 RNA concentrations follow symptom onset gathered by retrospective interview of patients but precedes clinical test results. Additionally, a near

complete (98.5%) SARS-CoV-2 genome sequence was determined from the wastewater and use phylogenetic analysis to infer viral ancestry. Collectively, this work demonstrates how wastewater can be used as a proxy to monitor viral prevalence in the community and how genome sequencing can be used for genotyping viral strains circulating in a community.

Reference

Nemudryi, Artem, Anna Nemudraia, Kevin Surya, Tanner Wiegand, Murat Buyukyoruk, Royce Wilkinson, and Blake Wiedenheft. "Temporal detection and phylogenetic assessment of SARS-CoV-2 in municipal wastewater." *medRxiv* (2020).

Publication Date: Aug 28, 2020

MHC class II transactivator CIITA induces cell resistance to Ebola virus and SARS-like coronaviruses

Recent outbreaks of Ebola virus (EBOV) and SARS-CoV-2 have exposed our limited therapeutic options and poor understanding of cellular mechanisms that block viral infections. Using a transposon-mediated gene-activation screen in human cells, we identify that the MHC class II transactivator (CIITA) has antiviral activity against EBOV. CIITA induces resistance by activating expression of the p41 isoform of invariant chain CD74, which inhibits viral entry by blocking cathepsin-mediated processing of the Ebola glycoprotein (EboGP). We further show that CD74 p41 can block the endosomal entry pathway of coronaviruses, including SARS-CoV-2. These data therefore implicate CIITA and CD74 in host defense against a range of viruses, and identify an additional function of these proteins beyond their canonical roles in antigen presentation. For more details, read the reference given below.

Reference

Bruchez, Anna, Ky Sha, Joshua Johnson, Li Chen, Caroline Stefani, Hannah McConnell, Lea Gaucherand et al. "MHC class II transactivator CIITA induces cell resistance to Ebola virus and SARS-like coronaviruses." *Science* (2020) (I.F.: 41.845).

Serial interval of SARS-CoV-2 was shortened over time by nonpharmaceutical interventions

Studies of novel coronavirus disease 2019 (COVID-19), which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), have reported varying estimates of epidemiological parameters, including serial interval distributions—*i.e.*, the time between illness onset in successive cases in a transmission chain—and reproduction numbers. By compiling a line-list database of transmission pairs in mainland China, we show that mean serial intervals of COVID-19 shortened substantially from 7.8 to 2.6 days within a month (9 January to 13 February 2020). This change was driven by enhanced nonpharmaceutical interventions, particularly case isolation. We also show that using real-time estimation of serial intervals allowing for variation over time provides more accurate estimates of reproduction numbers than using conventionally fixed serial interval distributions. These findings could improve our ability to assess transmission dynamics, forecast future incidence, and estimate the impact of control measures.

Reference

Ali, Sheikh Taslim, Lin Wang, Eric HY Lau, Xiao-Ke Xu, Zhanwei Du, Ye Wu, Gabriel M. Leung, and Benjamin J. Cowling. "Serial interval of SARS-CoV-2 was shortened over time by nonpharmaceutical interventions." *Science* 369, no. 6507 (2020): 1106-1109 (I.F.: 41.845).

Structural basis of a shared antibody response to SARS-CoV-2

Molecular understanding of neutralizing antibody responses to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) could accelerate vaccine design and drug discovery. We analyzed 294 anti-SARS-CoV-2 antibodies and found that immunoglobulin G heavy-chain variable region 3-53 (IGHV3-53) is the most frequently used IGHV gene for targeting the receptor-binding domain (RBD) of the spike protein. Co-crystal structures of two IGHV3-53–neutralizing antibodies with RBD, with or without Fab CR3022, at 2.33- to 3.20-angstrom resolution revealed that the germline-encoded residues dominate recognition of the angiotensin I converting enzyme 2 (ACE2)–binding site. This binding mode limits the IGHV3-53 antibodies to short complementarity-

determining region H3 loops but accommodates light-chain diversity. These IGHV3-53 antibodies show minimal affinity maturation and high potency, which is promising for vaccine design. Knowledge of these structural motifs and binding mode should facilitate the design of antigens that elicit this type of neutralizing response.

Reference

Yuan, Meng, Hejun Liu, Nicholas C. Wu, Chang-Chun D. Lee, Xueyong Zhu, Fangzhu Zhao, Deli Huang et al. "Structural basis of a shared antibody response to SARS-CoV-2." *Science* 369, no. 6507 (2020): 1119-1123 (I.F.: 41.845).

EDITORIAL

Publication Date: Sep 02, 2020

Continuous on-body sensing for the COVID-19 pandemic: Gaps and opportunities

There As of 20 June 2020, the Center for Disease Control's tabulations show more than 2.2 million recorded cases of coronavirus disease 2019 (COVID-19) and nearly 120,000 in deaths in the United States. Infected patients present with a wide range of symptoms, from completely asymptomatic to rapidly progressive pneumonia leading to death. Rigorous and widespread testing remains a critical component of strategies for containing this pandemic. The limited availability of molecular diagnostics constrains the use of these technologies to those who present with disease. The current gold standards rely on detection of viral RNA, typically by reverse transcription polymerase chain reaction (RT-PCR), but these approaches, as commonly implemented, have notable disadvantages. First, the nasopharyngeal swab is uncomfortable and may not be tolerated well by all patients, particularly children or the elderly. Second, false-negative test results remain a significant concern, with some RT-PCR tests exhibiting false-negative rates as high as 29%. Third, swab samples must be collected by trained staff to avoid false negatives or inconclusive tests. Fourth, samples must be transported via viral medium to centralized laboratory facilities, where transport delays from rural or remote areas can reach 48 hours or longer. Alternative tests based on antibodies offer some promise, but the appearance of antibodies [immunoglobulin M (IgM) and IgG] can lag weeks to months after the initial exposure. Furthermore, positive antibody titers may potentially only reflect prior exposure as opposed to protective immunity. Emerging evidence suggests that re-infection by endemic coronaviruses is not atypical, thereby adding complications to protocols for follow-up molecular testing. The net result is a continuing gap between widespread population-level testing and the availability of tests that is likely to persist for the foreseeable future. These circumstances motivate the development of complementary technologies for diagnosing and monitoring COVID-19 infections.

Reference

<https://advances.sciencemag.org/content/6/36/eabd4794>

COMMENT

Publication Date: Aug 27, 2020

COVID-19 vaccine trials should seek worthwhile efficacy

Three issues are crucial in planning COVID-19 vaccine trials: (1) whether to demand not only proof of some vaccine efficacy but also proof of worthwhile efficacy; (2) whether the initial trials of vaccine against placebo should prioritise not only single-vaccine trials but also a multivaccine trial; and (3) whether to assess safety, protection against severe disease, and duration of protection by continuing blinded follow-up of the vaccine and placebo groups after definite evidence of short-term efficacy has emerged, but before an effective vaccine has been deployed locally in the general population. The world needs efficient, speedy, and reliable evaluation of many candidate vaccines against COVID-19. There is a danger that political and economic pressures for rapid introduction of a COVID-19 vaccine could lead to widespread deployment of a vaccine that is in reality only weakly effective (e.g., reducing COVID-19 incidence by only 10–20%), perhaps because of a misleadingly promising result from an underpowered trial. Deployment of a weakly effective vaccine could actually worsen the COVID-19 pandemic if authorities wrongly assume it causes a substantial reduction in risk, or if vaccinated individuals wrongly believe they are immune, hence reducing implementation of, or compliance with, other COVID-19 control measures. Deployment of a marginally effective vaccine could also interfere with the evaluation of other vaccines, as subsequent vaccines would then have to be compared with it rather than with a placebo. For a vaccine superior to the weakly effective vaccine, the increased sample size required could delay recognition of its efficacy. More importantly, if the weak vaccine is compared against an even weaker vaccine, the statistical criteria used to analyse non-inferiority trials could well endorse the even weaker vaccine as being non-inferior (so-called bio-creep). The criteria used to define a successful vaccine in the initial clinical trials of vaccination versus placebo should therefore be strict enough to protect against the risk of a weakly effective vaccine being deployed, especially since there are already many candidate vaccines against COVID-19 to be tested,² providing many chances to overestimate efficacy. Hence, the initial trials comparing COVID-19

vaccines versus placebo should seek reliable evidence not only of some efficacy but of worthwhile efficacy. For more details, read the link given below.

Reference

[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)31821-3/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31821-3/fulltext)