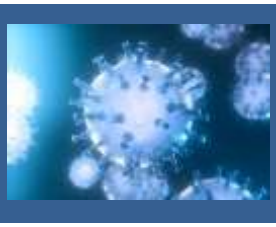

RESEARCH PUBLICATIONS

Publication Date: Mar 31, 2021

Alterations in T and B cell function persist in convalescent COVID-19 patients

Abstract

Background: Emerging studies indicate that some COVID-19 patients suffer from persistent symptoms including breathlessness and chronic fatigue; however the long-term immune response in these patients presently remains ill-defined.

Methods: The phenotypic and functional characteristics of B and T cells in hospitalised COVID-19 patients were described during acute disease and at 3-6 months of convalescence.

Findings: It was reported that the alterations in B cell subsets observed in acute COVID-19 patients were largely recovered in convalescent patients. In contrast, T cells from convalescent patients displayed continued alterations with persistence of a cytotoxic programme evident in CD8+ T cells as well as elevated production of type-1 cytokines and IL-17. Interestingly, B cells from patients with acute COVID-19 displayed an IL-6/IL-10 cytokine imbalance in response to toll-like receptor activation, skewed towards a pro-inflammatory phenotype. Whereas the frequency of IL-6+ B cells was restored in convalescent patients irrespective of clinical outcome, recovery of IL-10+ B cells was associated with resolution of lung pathology.

Conclusions: The data detail lymphocyte alterations in previously hospitalized COVID-19 patients up to 6 months following hospital discharge and identify 3 subgroups of convalescent patients based on distinct lymphocyte phenotypes, with one subgroup associated with poorer clinical outcome. It was proposed that alterations in B and T cell function following hospitalisation with COVID-19 could impact longer term immunity and contribute to some persistent symptoms observed in convalescent COVID-19 patients.

Reference

https://www.cell.com/med/fulltext/S2666-6340(21)00115-X

Simultaneous detection and mutation surveillance of SARS-CoV-2 and co-infections of multiple respiratory viruses by Rapid field-deployable sequencing

Abstract

Background: Strategies for monitoring the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections are crucial for combating the pandemic. Detection and mutation surveillance of SARS-CoV-2 and other respiratory viruses require separate and complex workflows that rely on highly-specialized facilities, personnel, and reagents. To date, no method can rapidly diagnose multiple viral infections and determine variants in a high-throughput manner.

Methods: A method was described for multiplex isothermal amplification-based sequencing and real-time analysis of multiple viral genomes, termed NIRVANA. It can simultaneously detect SARS-CoV-2, influenza A, human adenovirus, and human coronavirus, and monitor mutations for up to 96 samples in real-time.

Findings: NIRVANA showed high sensitivity and specificity for SARS-CoV-2 in 70 clinical samples with a detection limit of 20 viral RNA copies per μl of extracted nucleic acid. It also detected the influenza A co-infection in two samples. The variant analysis results of SARS-CoV-2 positive samples mirror the epidemiology of COVID-19. Additionally, NIRVANA could simultaneously detect SARS-CoV-2 and PMMoV (an omnipresent virus and water quality indicator) in municipal wastewater samples.

Conclusions: NIRVANA provides high-confidence detection of both SARS-CoV-2 and other respiratory viruses and mutation surveillance of SARS-CoV-2 on the fly. It was expected to offer a promising solution for rapid field-deployable detection and mutational surveillance of pandemic viruses.

Reference

https://www.cell.com/med/fulltext/S2666-6340(21)00117-3

SARS-CoV-2 prevalence associated to low socioeconomic status and overcrowding in an LMIC megacity: A population-based seroepidemiological survey in Lima, Peru

Abstract

Background: Worldwide, Peru has one of the highest infection fatality rates of COVID-19, and its capital city, Lima, accumulates roughly 50% of diagnosed cases. Despite surveillance efforts to assess the extent of the pandemic, reported cases and deaths only capture a fraction of its impact due to COVID-19′s broad clinical spectrum. This study aimed to estimate the seroprevalence of SARS-CoV-2 in Lima, stratified by age, sex, region, socioeconomic status (SES), overcrowding, and symptoms.

Methods: A multi-stage, population-based serosurvey was conducted in Lima, between June 28th and July 9th, 2020, after 115 days of the index case and after the first peak cases. Whole blood samples were collected by finger-prick and applied a structured questionnaire. A point-of-care rapid serological test assessed IgM and IgG antibodies against SARS-CoV-2. Seroprevalence estimates were adjusted by sampling weights and test performance. Additionally, RT-PCR molecular assays were performed to seronegatives and estimated the infection prevalence.

Findings: 3212 Participants were enrolled from 797 households and 241 sample clusters from Lima in the analysis. The SARS-CoV-2 seroprevalence was 20·8% (95%CI 17·2–23·5), and the prevalence was 25·2% (95%CI 22·5–28·2). Seroprevalence was equally distributed by sex (aPR=0·96 [95%CI 0·85–1·09, p = 0·547]) and across all age groups, including ≥60 versus ≤11 years old (aPR=0·96 [95%CI 0·73–1·27, p = 0·783]). A gradual decrease in SES was associated with higher seroprevalence (aPR=3·41 [95%CI 1·90–6·12, p<0·001] in low SES). Also, a gradual increase in the overcrowding index was associated with higher seroprevalence (aPR=1·99 [95%CI 1·41–2·81, p<0·001] in the fourth quartile). Seroprevalence was also associated with contact with a suspected or confirmed COVID-19 case, whether a household member (48·9%, aPR=2·67 [95%CI 2·06–3·47, p<0·001]), other family members (27·3%, aPR=1·66 [95%CI 1·15–2·40, p = 0·008]) or a workmate (34·1%, aPR=2·26 [95%CI 1·53–3·35, p<0·001]). More than half of seropositive participants reported never having had symptoms (56·1%, 95% CI 49·7–62·3).

Interpretation: This first estimate of SARS-CoV-2 seroprevalence in Lima shows an intense transmission scenario, despite the government's numerous interventions early established. Susceptibles across age groups show that physical distancing interventions must not be relaxed. SES and overcrowding households are associated with seroprevalence. This study highlights the importance of considering the existing social inequalities for implementing the response to control transmission in low- and middle-income countries.

Reference

https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00081-X/fulltext

Prioritising COVID-19 vaccination in changing social and epidemiological landscapes: A mathematical modelling study

Abstract

Background: During the COVID-19 pandemic, authorities must decide which groups to prioritise for vaccination in a shifting social–epidemiological landscape in which the success of large-scale non-pharmaceutical interventions requires broad social acceptance. It was aimed to compare projected COVID-19 mortality under four different strategies for the prioritisation of SARS-CoV-2 vaccines.

Methods: A coupled social–epidemiological model of SARS-CoV-2 transmission was developed in which social and epidemiological dynamics interact with one another. It was modelled how population adherence to non-pharmaceutical interventions responds to case incidence. In the model, schools and workplaces are also closed and reopened on the basis of reported cases. The model was parameterised with data on COVID-19 cases and mortality, SARS-CoV-2 seroprevalence, population mobility, and demography from Ontario, Canada (population 14·5 million). Disease progression parameters came from the SARS-CoV-2 epidemiological literature. A vaccine was assumed with 75% efficacy against disease and transmissibility. It was compared that vaccinating those aged 60 years and older first (oldest-first strategy), vaccinating those younger than 20 years first (youngest-first strategy), vaccinating uniformly by age (uniform strategy), and a novel contact-based strategy. The latter three strategies interrupt transmission, whereas the first targets a vulnerable group to reduce disease.

Vaccination rates ranged from 0·5% to 5% of the population per week, beginning on either Jan 1 or Sept 1, 2021.

Findings: Case notifications, non-pharmaceutical intervention adherence, and lockdown undergo successive waves that interact with the timing of the vaccine programme to determine the relative effectiveness of the four strategies. Transmission-interrupting strategies become relatively more effective with time as herd immunity builds. The model predicts that, in the absence of vaccination, 72 000 deaths (95% credible interval 40 000–122 000) would occur in Ontario from Jan 1, 2021, to March 14, 2025, and at a vaccination rate of 1·5% of the population per week, the oldest-first strategy would reduce COVID-19 mortality by 90·8% on average (followed by 89·5% in the uniform, 88·9% in the contact-based, and 88·2% in the youngest-first strategies). 60 000 deaths (31 000–108 000) would occur from Sept 1, 2021, to March 14, 2025, in the absence of vaccination, and the contact-based strategy would reduce COVID-19 mortality by 92·6% on average (followed by 92·1% in the uniform, 91·0% in the oldest-first, and 88·3% in the youngest-first strategies) at a vaccination rate of 1·5% of the population per week.

Interpretation: The most effective vaccination strategy for reducing mortality due to COVID-19 depends on the time course of the pandemic in the population. For later vaccination start dates, use of SARS-CoV-2 vaccines to interrupt transmission might prevent more deaths than prioritising vulnerable age groups.

Reference

https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00057-8/fulltext

Safety and efficacy of favipiravir versus hydroxychloroquine in management of COVID-19: A randomised controlled trial

Abstract

Favipiravir is considered a potential treatment for COVID-19 due its efficacy against different viral infections. It was aimed to explore the safety and efficacy of favipiravir in treatment of COVID-19 mild and moderate cases. It was randomized-controlled open-label interventional phase 3 clinical trial [NCT04349241]. 100 patients were recruited from 18th April till 18th May. 50 patients received favipiravir 3200 mg at day 1 followed by 600 mg twice (day 2–day 10). 50 patients received hydroxychloroquine 800 mg at

day 1 followed by 200 mg twice (day 2–10) and oral oseltamivir 75 mg/12 h/day for 10 days. Patients were enrolled from Ain Shams University Hospital and Assiut University Hospital. Both arms were comparable as regards demographic characteristics and comorbidities. The average onset of SARS-CoV-2 PCR negativity was 8.1 and 8.3 days in HCQ-arm and favipiravir-arm respectively. 55.1% of those on HCQ-arm turned PCR negative at/or before 7th day from diagnosis compared to 48% in favipiravir-arm ($p = 0.7$). 4 patients in FVP arm developed transient transaminitis on the other hand heartburn and nausea were reported in about 20 patients in HCQ-arm. Only one patient in HCQ-arm died after developing acute myocarditis resulted in acute heart failure. Favipiravir is a safe effective alternative for hydroxychloroquine in mild or moderate COVID-19 infected patients.

Reference

https://www.nature.com/articles/s41598-021-85227-0

A method for detection of SARS-CoV-2 RNA in healthy human stool: A validation study

Abstract

Background: Faecal shedding of SARS-CoV-2 has raised concerns about transmission through faecal microbiota transplantation procedures. Validation parameters of authorised tests for SARS-CoV-2 RNA detection in respiratory samples are described in product labelling, whereas the published methods for SARS-CoV-2 detection from faecal samples have not permitted a robust description of the assay parameters. It was aimed to develop and validate a test specifically for detection of SARS-CoV-2 in human stool.

Methods: In this validation study, performance characteristics of a reverse transcriptase real-time PCR (RT-rtPCR) test for detection of SARS-CoV-2 in human stool specimens were evaluated by spiking stool with inactivated SARS-CoV-2 material. A modified version of the US Centers for Disease Control and Prevention RT-rtPCR SARS-CoV-2 test was used for detection of viral RNA. Analytical sensitivity was evaluated in freshly spiked stool by testing two-fold dilutions in replicates of 20. Masked samples were tested by a second laboratory to evaluate interlaboratory reproducibility. Short-term (7-day) stability of viral RNA in stool samples was assessed with four different stool

storage buffers (phosphate-buffered saline, Cary-Blair medium, Stool Transport and Recovery [STAR] buffer, and DNA/RNA Shield) kept at −80°C, 4°C, and ambient temperature (approximately 21°C). We also tested clinical stool and anal swab specimens from patients who were SARS-CoV-2 positive by nasopharyngeal testing.

Findings: The lower limit of detection of the assay was found to be 3000 viral RNA copies per g of original stool sample, with 100% detection across 20 replicates assessed at this concentration. Analytical sensitivity was diminished by approximately two times after a single freeze-thaw cycle at −80°C. At 100 times the limit of detection, spiked samples were generally stable in all four stool storage buffers tested for up to 7 days, with maximum changes in mean threshold cycle values observed at −80°C storage in Cary-Blair medium (from 29·4 [SD 0·27] at baseline to 30·8 [0·17] at day 7; p<0·0001), at 4°C storage in DNA/RNA Shield (from 28·5 [0·15] to 29·8 [0·09]; p=0·0019), and at ambient temperature in STAR buffer (from 30·4 [0·24] to 32·4 [0·62]; p=0·0083). 30 contrived SARS-CoV-2 samples were tested by a second laboratory and were correctly identified as positive or negative in at least one of two rounds of testing. Additionally, SARS-CoV-2 RNA was detected using this assay in the stool and anal swab specimens of 11 of 23 individuals known to be positive for SARS-CoV-2.

Interpretation: This is a sensitive and reproducible assay for detection of SARS-CoV-2 RNA in human stool, with potential uses in faecal microbiota transplantation donor screening, sewage monitoring, and further research into the effects of faecal shedding on the epidemiology of the COVID-19 pandemic.

Reference

https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247(21)00059-8/fulltext

Risk factors on admission associated with hospital length of stay in patients with COVID-19: A retrospective cohort study

Abstract

Treating patients with COVID-19 is expensive, thus it is essential to identify factors on admission associated with hospital length of stay (LOS) and provide a risk assessment for clinical treatment. To address this, we conduct a retrospective study, which involved patients with laboratory-confirmed COVID-19 infection in Hefei, China and being

discharged between January 20 2020 and March 16 2020. Demographic information, clinical treatment, and laboratory data for the participants were extracted from medical records. A prolonged LOS was defined as equal to or greater than the median length of hospitable stay. The median LOS for the 75 patients was 17 days (IQR 13–22). We used univariable and multivariable logistic regressions to explore the risk factors associated with a prolonged hospital LOS. Adjusted odds ratios (aORs) and 95% confidence intervals (CIs) were estimated. The median age of the 75 patients was 47 years. Approximately 75% of the patients had mild or general disease. The univariate logistic regression model showed that female sex and having a fever on admission were significantly associated with longer duration of hospitalization. The multivariate logistic regression model enhances these associations. Odds of a prolonged LOS were associated with male sex (aOR 0.19, 95% CI 0.05–0.63, $p = 0.01$), having fever on admission (aOR 8.27, 95% CI 1.47–72.16, $p = 0.028$) and pre-existing chronic kidney or liver disease (aOR 13.73 95% CI 1.95–145.4, $p = 0.015$) as well as each 1-unit increase in creatinine level (aOR 0.94, 95% CI 0.9–0.98, $p = 0.007$). It was also found that a prolonged LOS was associated with increased creatinine levels in patients with chronic kidney or liver disease ($p < 0.001$). In conclusion, female sex, fever, chronic kidney or liver disease before admission and increasing creatinine levels were associated with prolonged LOS in patients with COVID-19.

Reference

https://www.nature.com/articles/s41598-021-86853-4

Gender associates with both susceptibility to infection and pathogenesis of SARS-CoV-2 in Syrian hamster

Abstract

Epidemiological studies of the COVID-19 patients have suggested the male bias in outcomes of lung illness. To experimentally demonstrate the epidemiological results, animal studies were performed to infect male and female Syrian hamsters with SARS-CoV-2. Remarkably, high viral titer in nasal washings was detectable in male hamsters who presented symptoms of weight loss, weakness, piloerection, hunched back and abdominal respiration, as well as severe pneumonia, pulmonary edema, consolidation, and fibrosis. In contrast with the males, the female hamsters showed much lower

shedding viral titers, moderate symptoms, and relatively mild lung pathogenesis. The obvious differences in the susceptibility to SARS-CoV-2 and severity of lung pathogenesis between male and female hamsters provided experimental evidence that SARS-CoV-2 infection and the severity of COVID-19 are associated with gender.

Reference

https://www.nature.com/articles/s41392-021-00552-0

Computational drug repurposing study elucidating simultaneous inhibition of entry and replication of novel corona virus by Grazoprevir

Abstract

Outcomes of various clinical studies for the coronavirus disease 2019 (COVID-19) treatment indicated that the drug acts via inhibition of multiple pathways (targets) is likely to be more successful and promising. Keeping this hypothesis intact, the present study describes for the first-time, Grazoprevir, an FDA approved anti-viral drug primarily approved for Hepatitis C Virus (HCV), mediated multiple pathway control via synergistic inhibition of viral entry targeting host cell Angiotensin-Converting Enzyme 2 (ACE-2)/transmembrane serine protease 2 (TMPRSS2) and viral replication targeting RNA-dependent RNA polymerase (RdRP). Molecular modeling followed by in-depth structural analysis clearly demonstrated that Grazoprevir interacts with the key residues of these targets. Futher, Molecular Dynamics (MD) simulations showed stability and burial of key residues after the complex formation. Finally, Molecular Mechanics Poisson-Boltzmann Surface Area (MM-PBSA) analysis identified the governing force of drug-receptor interactions and stability. Thus, we believe that Grazoprevir could be an effective therapeutics for the treatment of the COVID-19 pandemic with a promise of unlikely drug resistance owing to multiple inhibitions of eukaryotic and viral proteins, thus warrants further clinical studies.

Reference

https://www.nature.com/articles/s41598-021-86712-2

Antibody evasion by the P.1 strain of SARS-CoV-2

Abstract

Terminating the SARS-CoV-2 pandemic relies upon pan-global vaccination. Current vaccines elicit neutralizing antibody responses to the virus spike derived from early isolates. However, new strains have emerged with multiple mutations: P.1 from Brazil, B.1.351 from South Africa and B.1.1.7 from the UK (12, 10 and 9 changes in the spike respectively). All have mutations in the ACE2 binding site with P.1 and B.1.351 having a virtually identical triplet: E484K, K417N/T and N501Y, which we show confer similar increased affinity for ACE2. We show that, surprisingly, P.1 is significantly less resistant to naturally acquired or vaccine induced antibody responses than B.1.351 suggesting that changes outside the RBD impact neutralisation. Monoclonal antibody 222 neutralises all three variants despite interacting with two of the ACE2 binding site mutations, we explain this through structural analysis and use the 222 light chain to largely restore neutralization potency to a major class of public antibodies.

Reference

https://www.cell.com/cell/fulltext/S0092-8674(21)00428-1

Efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine against SARS-CoV-2 variant of concern 202012/01 (B.1.1.7): An exploratory analysis of a randomised controlled trial

Abstract

Background: A new variant of SARS-CoV-2, B.1.1.7, emerged as the dominant cause of COVID-19 disease in the UK from November, 2020. A post-hoc analysis of the efficacy of the adenoviral vector vaccine, ChAdOx1 nCoV-19 (AZD1222), was reported against this variant.

Methods: Volunteers (aged ≥18 years) who were enrolled in phase 2/3 vaccine efficacy studies in the UK, and who were randomly assigned (1:1) to receive ChAdOx1 nCoV-19 or a meningococcal conjugate control (MenACWY) vaccine, provided upper airway swabs on a weekly basis and also if they developed symptoms of COVID-19 disease (a cough, a fever of 37·8°C or higher, shortness of breath, anosmia, or ageusia). Swabs

were tested by nucleic acid amplification test (NAAT) for SARS-CoV-2 and positive samples were sequenced through the COVID-19 Genomics UK consortium. Neutralising antibody responses were measured using a live-virus microneutralisation assay against the B.1.1.7 lineage and a canonical non-B.1.1.7 lineage (Victoria). The efficacy analysis included symptomatic COVID-19 in seronegative participants with a NAAT positive swab more than 14 days after a second dose of vaccine. Participants were analysed according to vaccine received. Vaccine efficacy was calculated as 1 − relative risk (ChAdOx1 nCoV-19 vs MenACWY groups) derived from a robust Poisson regression model. This study is continuing and is registered with ClinicalTrials.gov, NCT04400838, and ISRCTN, 15281137.

Findings: Participants in efficacy cohorts were recruited between May 31 and Nov 13, 2020, and received booster doses between Aug 3 and Dec 30, 2020. Of 8534 participants in the primary efficacy cohort, 6636 (78%) were aged 18–55 years and 5065 (59%) were female. Between Oct 1, 2020, and Jan 14, 2021, 520 participants developed SARS-CoV-2 infection. 1466 NAAT positive nose and throat swabs were collected from these participants during the trial. Of these, 401 swabs from 311 participants were successfully sequenced. Laboratory virus neutralisation activity by vaccine-induced antibodies was lower against the B.1.1.7 variant than against the Victoria lineage (geometric mean ratio 8·9, 95% CI 7·2–11·0). Clinical vaccine efficacy against symptomatic NAAT positive infection was 70·4% (95% CI 43·6–84·5) for B.1.1.7 and 81·5% (67·9–89·4) for non-B.1.1.7 lineages.

Interpretation: ChAdOx1 nCoV-19 showed reduced neutralisation activity against the B.1.1.7 variant compared with a non-B.1.1.7 variant *in vitro*, but the vaccine showed efficacy against the B.1.1.7 variant of SARS-CoV-2.

Reference

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00628-0/fulltext

Emergence and rapid transmission of SARS-CoV-2 B.1.1.7 in the United States

Abstract

The highly transmissible B.1.1.7 variant of SARS-CoV-2, first identified in the United Kingdom, has gained a foothold across the world. Using S gene target failure (SGTF)

and SARS-CoV-2 genomic sequencing, we investigated the prevalence and dynamics of this variant in the United States (U.S.), tracking it back to its early emergence. It was found that while the fraction of B.1.1.7 varied by state, the variant increased at a logistic rate with a roughly weekly doubling rate and an increased transmission of 40-50%. We revealed several independent introductions of B.1.1.7 into the U.S. as early as late November 2020, with community transmission spreading it to most states within months. It was shown that the U.S. is on a similar trajectory as other countries where B.1.1.7 became dominant, requiring immediate and decisive action to minimize COVID-19 morbidity and mortality.

Reference

https://www.cell.com/cell/fulltext/S0092-8674(21)00383-4

TOP1 inhibition therapy protects against SARS-CoV-2-induced lethal inflammation

Abstract

The ongoing pandemic caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is currently affecting millions of lives worldwide. Large retrospective studies indicate that an elevated level of inflammatory cytokines and pro-inflammatory factors are associated with both increased disease severity and mortality. Here, using multidimensional epigenetic, transcriptional, *in vitro* and *in vivo* analyses, we report that Topoisomerase 1 (TOP1) inhibition suppresses lethal inflammation induced by SARS-CoV-2. Therapeutic treatment with two doses of Topotecan (TPT), a FDA-approved TOP1 inhibitor, suppresses infection-induced inflammation in hamsters. TPT treatment as late as four days post-infection reduces morbidity and rescues mortality in a transgenic mouse model. These results support the potential of TOP1 inhibition as an effective host-directed therapy against severe SARS-CoV-2 infection. TPT and its derivatives are inexpensive clinical-grade inhibitors available in most countries. Clinical trials are needed to evaluate the efficacy of repurposing TOP1 inhibitors for severe COVID-19 in humans.

Reference

https://www.cell.com/cell/fulltext/S0092-8674(21)00382-2

Assessment of pulmonary arterial circulation 3 months after hospitalization for SARS-CoV-2 pneumonia: Dual-energy CT (DECT) angiographic study in 55 patients

Abstract

Background: During COVID-19, the main manifestations of the disease are not only pneumonia but also coagulation disorders. The purpose of this study was to evaluate pulmonary vascular abnormalities 3 months after hospitalization for SARS-CoV-2 pneumonia in patients with persistent respiratory symptoms.

Methods: Among the 320 patients who participated in a systematic follow-up 3 months after hospitalization, 76 patients had residual symptoms justifying a specialized follow-up in the department of pulmonology. Among them, dual-energy CT angiography (DECTA) was obtained in 55 patients.

Findings: The 55 patients had partial (n = 40; 72.7%) or complete (n = 15; 27.3%) resolution of COVID-19 lung infiltration. DECTA was normal in 52 patients (52/55; 94.6%) and showed endoluminal filling defects in 3 patients (3/55; 5.4%) at the level of one (n = 1) and two (n = 1) segmental arteries of a single lobe and within central and peripheral arteries (n = 1). DECT lung perfusion was rated as non-interpretable (n = 2;3.6%), normal (n = 17; 30.9%) and abnormal (n = 36; 65.5%), the latter group comprising 32 patients with residual COVID-19 opacities (32/36; 89%) and 4 patients with normal lung parenchyma (4/36; 11%). Perfusion abnormalities consisted of (a) patchy defects (30/36; 83%), (b) PE-type defects (6/36; 16.6%) with (n = 1) or without proximal thrombosis (n = 5); and (c) focal areas of hypoperfusion (2/36; 5.5%). Increased perfusion was seen in 15 patients, always matching GGOs, bands and/or vascular tree-in- bud patterns.

Interpretation: DECT depicted proximal arterial thrombosis in 5.4% of patients and perfusion abnormalities suggestive of widespread microangiopathy in 65.5% of patients. Lung microcirculation was abnormal in 4 patients with normal lung parenchyma.

Reference

https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00058-4/fulltext

The impact of viremia on organ failure, biomarkers and mortality in a Swedish cohort of critically ill COVID-19 patients

Abstract

The spread of virus *via* the blood stream has been suggested to contribute to extra-pulmonary organ failure in Coronavirus disease 2019 (COVID-19). We assessed SARS-CoV-2 RNAemia (RNAemia) and the association between RNAemia and inflammation, organ failure and mortality in critically ill COVID-19 patients. It was included that all patients with PCR verified COVID-19 and consent admitted to ICU. SARS-CoV-2 RNA copies above 1000/ml measured by PCR in plasma was defined as RNAemia and used as surrogate for viremia. In this cohort of 92 patients 59 (64%) were invasively ventilated. RNAemia was found in 31 patients (34%). Hypertension and corticosteroid treatment was more common in patients with RNAemia. Extra-pulmonary organ failure biomarkers and the extent of organ failure were similar in patients with and without RNAemia, but the former group had more renal replacement therapy and higher mortality (26 vs 16%; 35 vs 16%, respectively, $p = 0.04$). RNAemia was not an independent predictor of death at 30 days after adjustment for age. SARS-CoV2 RNA copies in plasma is a common finding in ICU patients with COVID-19. Although viremia was not associated with extra pulmonary organ failure it was more common in patients who did not survive to 30 days after ICU admission.

Reference

https://www.nature.com/articles/s41598-021-86500-y

Peginterferon Lambda-1a for treatment of outpatients with uncomplicated COVID-19: A randomized placebo-controlled trial

Abstract

Type III interferons have been touted as promising therapeutics in outpatients with coronavirus disease 2019 (COVID-19). A randomized, single-blind, placebo-controlled trial (NCT04331899) was conducted in 120 outpatients with mild to moderate COVID-19 to determine whether a single, 180 mcg subcutaneous dose of Peginterferon Lambda-1a (Lambda) within 72 hours of diagnosis could shorten the duration of viral shedding (primary endpoint) or symptoms (secondary endpoint). In both the 60 patients receiving Lambda and 60 receiving placebo, the median time to cessation of viral shedding was 7

days (hazard ratio [HR] = 0.81; 95% confidence interval [CI] 0.56 to 1.19). Symptoms resolved in 8 and 9 days in Lambda and placebo, respectively, and symptom duration did not differ significantly between groups (HR 0.94; 95% CI 0.64 to 1.39). Both Lambda and placebo were well-tolerated, though liver transaminase elevations were more common in the Lambda vs. placebo arm (15/60 vs 5/60; p = 0.027). In this study, a single dose of subcutaneous Peginterferon Lambda-1a neither shortened the duration of SARS-CoV-2 viral shedding nor improved symptoms in outpatients with uncomplicated COVID-19.

Reference

https://www.nature.com/articles/s41467-021-22177-1

Replicating bacterium-vectored vaccine expressing SARS-CoV-2 Membrane and Nucleocapsid proteins protects against severe COVID-19-like disease in hamsters

Abstract

To generate an inexpensive readily manufactured COVID-19 vaccine, the LVS ΔcapB vector platform was employed, previously used to generate potent candidate vaccines against Select Agent diseases tularemia, anthrax, plague, and melioidosis. Vaccines expressing SARS-CoV-2 structural proteins are constructed using the LVS ΔcapB vector, a highly attenuated replicating intracellular bacterium, and evaluated for efficacy in golden Syrian hamsters, which develop severe COVID-19-like disease. Hamsters immunized intradermally or intranasally with a vaccine co-expressing the Membrane and Nucleocapsid proteins and challenged 5 weeks later with a high dose of SARS-CoV-2 are protected against severe weight loss and lung pathology and show reduced viral loads in the oropharynx and lungs. Protection correlates with anti-Nucleocapsid antibody. This potent vaccine should be safe; inexpensive; easily manufactured, stored, and distributed; and given the high homology between Membrane and Nucleocapsid proteins of SARS-CoV and SARS-CoV-2, potentially serve as a universal vaccine against the SARS subset of pandemic causing β-coronaviruses.

Reference

https://www.nature.com/articles/s41541-021-00321-8

SARS-CoV-2 in severe COVID-19 induces a TGF-β-dominated chronic immune response that does not target itself

Abstract

The pathogenesis of severe COVID-19 reflects an inefficient immune reaction to SARS-CoV-2. Here, at the single cell level, plasmablasts egressed into the blood we analyzed to study the dynamics of adaptive immune response in COVID-19 patients requiring intensive care. Before seroconversion in response to SARS-CoV-2 spike protein, peripheral plasmablasts display a type 1 interferon-induced gene expression signature; however, following seroconversion, plasmablasts lose this signature, express instead gene signatures induced by IL-21 and TGF-β, and produce mostly IgG1 and IgA1. In the sustained immune reaction from COVID-19 patients, plasmablasts shift to the expression of IgA2, thereby reflecting an instruction by TGF-β. Despite their continued presence in the blood, plasmablasts are not found in the lungs of deceased COVID-19 patients, nor does patient IgA2 binds to the dominant antigens of SARS-CoV-2. Our results thus suggest that, in severe COVID-19, SARS-CoV-2 triggers a chronic immune reaction that is instructed by TGF-β, and is distracted from itself.

Reference

https://www.nature.com/articles/s41467-021-22210-3

Integrated characterization of SARS-CoV-2 genome, microbiome, antibiotic resistance and host response from single throat swabs

Abstract

The ongoing coronavirus disease 2019 (COVID-19) pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, poses a severe threat to humanity. Rapid and comprehensive analysis of both pathogen and host sequencing data is critical to track infection and inform therapies. In this study, unbiased metatranscriptomic analysis of clinical samples were performed from COVID-19 patients using a recently developed RNA-seq library construction method (TRACE-seq), which utilizes tagmentation activity of Tn5 on RNA/DNA hybrids. This approach avoids the laborious and time-consuming steps in traditional RNA-seq procedure, and hence is fast, sensitive, and convenient. It was demonstrated that TRACE-seq allowed integrated characterization of full genome information of SARS-CoV-2, putative pathogens causing

coinfection, antibiotic resistance, and host response from single throat swabs. It was believed that the integrated information will deepen our understanding of pathogenesis and improve diagnostic accuracy for infectious diseases.

Reference

https://www.nature.com/articles/s41421-021-00248-3

Ivermectin reduces *in vivo* coronavirus infection in a mouse experimental model

Abstract

The objective of this study was to test the effectiveness of ivermectin for the treatment of mouse hepatitis virus (MHV), a type 2 family RNA coronavirus similar to SARS-CoV-2. Female BALB/cJ mice were infected with 6,000 PFU of MHV-A59 (group infected, $n = 20$) or infected and then immediately treated with a single dose of 500 µg/kg ivermectin (group infected + IVM, $n = 20$) or were not infected and treated with PBS (control group, $n = 16$). Five days after infection/treatment, the mice were euthanized and the tissues were sampled to assess their general health status and infection levels. Overall, the results demonstrated that viral infection induced typical MHV-caused disease, with the livers showing severe hepatocellular necrosis surrounded by a severe lymphoplasmacytic inflammatory infiltration associated with a high hepatic viral load (52,158 AU), while mice treated with ivermectin showed a better health status with a lower viral load (23,192 AU; $p < 0.05$), with only a few having histopathological liver damage ($p < 0.05$). No significant differences were found between the group infected + IVM and control group mice ($P = NS$). Furthermore, serum transaminase levels (aspartate aminotransferase and alanine aminotransferase) were significantly lower in the treated mice than in the infected animals. In conclusion, ivermectin diminished the MHV viral load and disease in the mice, being a useful model for further understanding this therapy against coronavirus diseases.

Reference

https://www.nature.com/articles/s41598-021-86679-0

Multivalent binding of the partially disordered SARS-CoV-2 nucleocapsid phosphoprotein dimer to RNA

Abstract

The nucleocapsid phosphoprotein N plays critical roles in multiple processes of the SARS-CoV-2 infection cycle: it protects and packages viral RNA in nucleocapsid assembly, interacts with the inner domain of spike protein in virion assembly, binds to structural membrane protein M during virion packaging and maturation, and binds to proteases causing replication of infective virus particle. Even with its importance, very limited biophysical studies are available on the N protein because of its high level of disorder, high propensity for aggregation and high susceptibility for autoproteolysis. Here we successfully prepare the N protein and a 1000 nucleotide fragment of viral RNA in large quantities and purity suitable for biophysical studies. A combination of biophysical and biochemical techniques demonstrates that the N protein is partially disordered and consists of an independently folded RNA binding domain and a dimerization domain, flanked by disordered linkers. The protein assembles as a tight dimer with a dimerization constant of sub micro molar, but can also form transient interactions with other N proteins facilitating larger oligomers. NMR studies on the ~100kDa dimeric protein identify a specific domain that binds 1-1000 RNA and show that the N/RNA complex remains highly disordered. Analytical ultracentrifugation, isothermal titration calorimetry, multi-angle light scattering, and cross-linking experiments identify a heterogeneous mixture of complexes with a core corresponding to at least 70 dimers of N bound to 1-1000 RNA. In contrast, very weak binding is detected with a smaller construct corresponding to the RNA binding domain using similar experiments. A model that explains the importance of the bivalent structure of N to its binding on multivalent sites of the viral RNA is presented.

Reference

https://www.cell.com/biophysj/fulltext/S0006-3495(21)00253-8

SARS-CoV2 Nsp16 activation mechanism and a cryptic pocket with pan-coronavirus antiviral potential

Abstract

Coronaviruses have caused multiple epidemics in the past two decades, in addition to the current COVID-19 pandemic that is severely damaging global health and the economy. Coronaviruses employ between twenty and thirty proteins to carry out their viral replication cycle including infection, immune evasion, and replication. Among these, nonstructural protein 16 (Nsp16), a 2'-O-methyltransferase, plays an essential role in immune evasion. Nsp16 achieves this by mimicking its human homolog, CMTr1, which methylates mRNA to enhance translation efficiency and distinguish self from other. Unlike human CMTr1, Nsp16 requires a binding partner, Nsp10, to activate its enzymatic activity. The requirement of this binding partner presents two questions that we investigate in this manuscript. First, how does Nsp10 activate Nsp16? While experimentally-derived structures of the active Nsp16/Nsp10 complex exist, structures of inactive, monomeric Nsp16 have yet to be solved. Therefore, it is unclear how Nsp10 activates Nsp16. Using over one millisecond of molecular dynamics simulations of both Nsp16 and its complex with Nsp10, we investigate how the presence of Nsp10 shifts Nsp16's conformational ensemble in order to activate it. Second, guided by this activation mechanism and Markov state models (MSMs), we investigate if Nsp16 adopts inactive structures with cryptic pockets that, if targeted with a small molecule, could inhibit Nsp16 by stabilizing its inactive state. After identifying such a pocket in SARS-CoV2 Nsp16, we show that this cryptic pocket also opens in SARS-CoV1 and MERS, but not in human CMTr1. Therefore, it may be possible to develop pan-coronavirus antivirals that target this cryptic pocket.

Reference

https://www.cell.com/biophysj/fulltext/S0006-3495(21)00254-X

Network-based virus-host interaction prediction with application to SARS-CoV-2

Abstract

COVID-19, caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), has quickly become a global health crisis since the first report of infection in December of 2019. However, the infection spectrum of SARS-CoV-2 and its

comprehensive protein-level interactions with hosts remain unclear. There is a massive amount of under-utilized data and knowledge about RNA viruses highly relevant to SARS-CoV-2 and proteins of their hosts. More in-depth and more comprehensive analyses of that knowledge and data can shed new insight into the molecular mechanisms underlying the COVID-19 pandemic and reveal potential risks. In this work, a multi-layer virus-host interaction network was constructed to incorporate these data and knowledge. A machine learning-based method was developed to predict virus-host interactions at both protein and organism levels. The approach revealed five potential infection targets of SARS-CoV-2 and 19 highly possible interactions between SARS-CoV-2 proteins and human proteins in the innate immune pathway.

Reference

https://www.cell.com/patterns/fulltext/S2666-3899(21)00062-3

The spatial landscape of lung pathology during COVID-19 progression

Abstract

Recent studies have provided insights into the pathology and immune response to coronavirus disease 2019 (COVID-19). However, thorough interrogation of the interplay between infected cells and the immune system at sites of infection is lacking. High parameter imaging mass cytometry was used targeting the expression of 36 proteins, to investigate at single cell resolution, the cellular composition and spatial architecture of human acute lung injury including SARS-CoV-2. This spatially resolved, single-cell data unravels the disordered structure of the infected and injured lung alongside the distribution of extensive immune infiltration. Neutrophil and macrophage infiltration are hallmarks of bacterial pneumonia and COVID-19, respectively. Evidence was provided that SARS-CoV-2 infects predominantly alveolar epithelial cells and induces a localized hyper-inflammatory cell state associated with lung damage. By leveraging the temporal range of COVID-19 severe fatal disease in relation to the time of symptom onset, we observe increased macrophage extravasation, mesenchymal cells, and fibroblasts abundance concomitant with increased proximity between these cell types as the disease progresses, possibly as an attempt to repair the damaged lung tissue. This spatially resolved single-cell data allowed us to develop a biologically interpretable landscape of lung pathology from a structural, immunological and clinical standpoint.

This spatial single-cell landscape enabled the pathophysiological characterization of the human lung from its macroscopic presentation to the single-cell, providing an important basis for the understanding of COVID-19, and lung pathology in general.

Reference

https://www.nature.com/articles/s41586-021-03475-6

Comprehensive transcriptomic analysis of COVID-19 blood, lung, and airway

Abstract

SARS-CoV2 is a previously uncharacterized coronavirus and causative agent of the COVID-19 pandemic. The host response to SARS-CoV2 has not yet been fully delineated, hampering a precise approach to therapy. To address this, we carried out a comprehensive analysis of gene expression data from the blood, lung, and airway of COVID-19 patients. The results indicate that COVID-19 pathogenesis is driven by populations of myeloid-lineage cells with highly inflammatory but distinct transcriptional signatures in each compartment. The relative absence of cytotoxic cells in the lung suggests a model in which delayed clearance of the virus may permit exaggerated myeloid cell activation that contributes to disease pathogenesis by the production of inflammatory mediators. The gene expression profiles also identify potential therapeutic targets that could be modified with available drugs. The data suggest that transcriptomic profiling can provide an understanding of the pathogenesis of COVID-19 in individual patients.

Reference

https://www.nature.com/articles/s41598-021-86002-x

Federated deep learning for detecting COVID-19 lung abnormalities in CT: A privacy-preserving multinational validation study

Abstract

Data privacy mechanisms are essential for rapidly scaling medical training databases to capture the heterogeneity of patient data distributions toward robust and generalizable machine learning systems. In the current COVID-19 pandemic, a major focus of artificial intelligence (AI) is interpreting chest CT, which can be readily used in the assessment and management of the disease. This paper demonstrates the feasibility of a federated

learning method for detecting COVID-19 related CT abnormalities with external validation on patients from a multinational study. 132 Patients were recruited from seven multinational different centers, with three internal hospitals from Hong Kong for training and testing, and four external, independent datasets from Mainland China and Germany, for validating model generalizability. It was also conducted case studies on longitudinal scans for automated estimation of lesion burden for hospitalized COVID-19 patients. It was explored the federated learning algorithms to develop a privacy-preserving AI model for COVID-19 medical image diagnosis with good generalization capability on unseen multinational datasets. Federated learning could provide an effective mechanism during pandemics to rapidly develop clinically useful AI across institutions and countries overcoming the burden of central aggregation of large amounts of sensitive data.

Reference

https://www.nature.com/articles/s41746-021-00431-6

A haemagglutination test for rapid detection of antibodies to SARS-CoV-2

Abstract

Serological detection of antibodies to SARS-CoV-2 is essential for establishing rates of seroconversion in populations, and for seeking evidence for a level of antibody that may be protective against COVID-19 disease. Several high-performance commercial tests have been described, but these require centralised laboratory facilities that are comparatively expensive, and therefore not available universally. Red cell agglutination tests do not require special equipment, are read by eye, have short development times, low cost and can be applied at the Point of Care. Here we describe a quantitative Haemagglutination test (HAT) for the detection of antibodies to the receptor binding domain of the SARS-CoV-2 spike protein. The HAT has a sensitivity of 90% and specificity of 99% for detection of antibodies after a PCR diagnosed infection. We will supply aliquots of the test reagent sufficient for ten thousand test wells free of charge to qualified research groups anywhere in the world.

Reference

https://www.nature.com/articles/s41467-021-22045-y

DNA methylation architecture of the ACE2 gene in nasal cells of children

Abstract

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has led to the global coronavirus disease 2019 (COVID-19) pandemic. SARS-CoV-2 enters cells *via* angiotensin-Converting Enzyme 2 (ACE2) receptors, highly expressed in nasal epithelium with parallel high infectivity. The nasal epigenome is in direct contact with the environment and could explain COVID-19 disparities by reflecting social and environmental influences on ACE2 regulation. Nasal swabs were collected from anterior nares of 547 children, measured DNA methylation (DNAm), and tested differences at 15 ACE2 CpGs by sex, age, race/ethnicity and epigenetic age. ACE2 CpGs were differentially methylated by sex with 12 sites having lower DNAm (mean = 12.71%) and 3 sites greater DNAm (mean = 1.45%) among females relative to males. We observed differential DNAm at 5 CpGs for Hispanic females (mean absolute difference = 3.22%) and lower DNAm at 8 CpGs for Black males (mean absolute difference = 1.33%), relative to white participants. Longer DNAm telomere length was associated with greater ACE2 DNAm at 11 and 13 CpGs among males (mean absolute difference = 7.86%) and females (mean absolute difference = 8.21%), respectively. Nasal ACE2 DNAm differences could contribute to our understanding COVID-19 severity and disparities reflecting upstream environmental and social influences. Findings need to be confirmed among adults and patients with risk factors for COVID-19 severity.

Reference

https://www.nature.com/articles/s41598-021-86494-7

Initial report of decreased SARS-CoV-2 viral load after inoculation with the BNT162b2 vaccine

Abstract

Beyond their substantial protection of individual vaccinees, coronavirus disease 2019 (COVID-19) vaccines might reduce viral load in breakthrough infection and thereby further suppress onward transmission. In this analysis of a real-world dataset of positive severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) test results after inoculation with the BNT162b2 messenger RNA vaccine, it was found that the viral load

was substantially reduced for infections occurring 12–37 d after the first dose of vaccine. These reduced viral loads hint at a potentially lower infectiousness, further contributing to vaccine effect on virus spread.

Reference

https://www.nature.com/articles/s41591-021-01316-7

Escape of SARS-CoV-2 501Y.V2 from neutralization by convalescent plasma

Abstract

SARS-CoV-2 variants of concern (VOC) have arisen independently at multiple locations and may reduce the efficacy of current vaccines targeting the spike glycoprotein. Here, using a live virus neutralization assay (LVNA), we compared neutralization of a non-VOC variant versus the 501Y.V2 variant using plasma collected from adults hospitalized with COVID-19 from two South African infection waves, with the second wave dominated by 501Y.V2 infections. Sequencing demonstrated that infections in first wave plasma donors were with viruses harbouring none of the 501Y.V2-defining mutations, except for one with the E484K mutation in the receptor binding domain. 501Y.V2 virus was effectively neutralized by plasma from second wave infections and first wave virus was effectively neutralized by first wave plasma. In cross-neutralization, 501Y.V2 virus was poorly neutralized by first wave plasma, with a 15.1-fold drop relative to 501Y.V2 neutralization by second wave plasma across participants. In contrast, second wave plasma cross-neutralization of first wave virus was more effective, showing only a 2.3-fold decline relative to first wave plasma neutralization of first wave virus. While, one plasma elicited by E484K alone was only tested, this potently neutralized both variants. The observed effective neutralization of first wave virus by 501Y.V2 infection elicited plasma provides preliminary evidence that vaccines based on VOC sequences could retain activity against other circulating SARS-CoV-2 lineages.

Reference

https://www.nature.com/articles/s41586-021-03471-w

Mass molecular testing for COVID19 using NGS-based technology and a highly scalable workflow

Abstract

Since the first reported case of the new coronavirus infection in Wuhan, China, researchers and governments have witnessed an unseen rise in the number of cases. Thanks to the rapid work of Chinese scientists, the pathogen now called SARS-CoV-2 has been identified and its whole genome was deposited in public databases by early January 2020. The availability of the genome has allowed researchers to develop Reverse Transcription—Polymerase Chain Reaction (RT-PCR) assays, which are now the gold-standard for molecular diagnosis of the respiratory syndrome COVID19. Because of the rising number of cases and rapid spreading, the world has been facing a shortage of RT-PCR supplies, especially the ones involved in RNA extraction. This has been a major bottleneck to increase testing capacity in many countries that do not significantly manufacture these supplies, such as Brazil. Additionally, RT-qPCR scalability is highly dependent on equipment that usually performs testing of 96 samples at a time. In this work, we describe a cost-effective molecular NGS-based test for diagnosis of COVID19, which uses a single-step RNA extraction and presents high scalability and accuracy when compared to the gold-standard RT-qPCR. A single run of the NGS-based test using the Illumina NextSeq 550 mid-end sequencing equipment is able to multiplex 1,536 patient's samples, providing individual semi-qualitative results (detected, not detected). Detected results are provided with fragments per million (FPM) values, which was demonstrated to correlate with RT-qPCR Cycle Threshold (CT) values. Besides, usage of the high-end Illumina Novaseq platform may yield diagnostic for up to 6144 samples in a single run. Performance results when compared with RT-qPCR show general accuracy of 96%, and 98% when only samples with CT values (gene N) lower than 30 are considered. We have also developed an online platform, termed VarsVID, to help test executors to easily scale testing numbers. Sample registering, wet-lab worksheets generation, sample sheet for sequencing and results' display are all features provided by VarsVID. Altogether, these results will contribute to control COVID19 pandemics.

Reference

https://www.nature.com/articles/s41598-021-86498-3

The SARS-CoV-2 nucleocapsid protein is dynamic, disordered, and phase separates with RNA

Abstract

The SARS-CoV-2 nucleocapsid (N) protein is an abundant RNA-binding protein critical for viral genome packaging, yet the molecular details that underlie this process are poorly understood. Here we combine single-molecule spectroscopy with all-atom simulations to uncover the molecular details that contribute to N protein function. N protein contains three dynamic disordered regions that house putative transiently-helical binding motifs. The two folded domains interact minimally such that full-length N protein is a flexible and multivalent RNA-binding protein. N protein also undergoes liquid-liquid phase separation when mixed with RNA, and polymer theory predicts that the same multivalent interactions that drive phase separation also engender RNA compaction. We offer a simple symmetry-breaking model that provides a plausible route through which single-genome condensation preferentially occurs over phase separation, suggesting that phase separation offers a convenient macroscopic readout of a key nanoscopic interaction.

Reference

https://www.nature.com/articles/s41467-021-21953-3

Publication Date: Mar 27, 2021

Cathepsin L plays a key role in SARS-CoV-2 infection in humans and humanized mice and is a promising target for new drug development

Abstract

To discover new drugs to combat COVID-19, an understanding of the molecular basis of SARS-CoV-2 infection is urgently needed. Here, for the first time, the crucial role of cathepsin L (CTSL) was reported in patients with COVID-19. The circulating level of CTSL was elevated after SARS-CoV-2 infection and was positively correlated with disease course and severity. Correspondingly, SARS-CoV-2 pseudovirus infection increased CTSL expression in human cells *in vitro* and human ACE2 transgenic mice *in vivo*, while CTSL overexpression, in turn, enhanced pseudovirus infection in human cells. CTSL functionally cleaved the SARS-CoV-2 spike protein and enhanced virus entry, as evidenced by CTSL overexpression and knockdown *in vitro* and application of

CTSL inhibitor drugs *in vivo*. Furthermore, amantadine, a licensed anti-influenza drug, significantly inhibited CTSL activity after SARS-CoV-2 pseudovirus infection and prevented infection both *in vitro* and *in vivo*. Therefore, CTSL is a promising target for new anti-COVID-19 drug development.

Reference

https://www.nature.com/articles/s41392-021-00558-8

Publication Date: Mar 26, 2021

***N*-Protein presents early in blood, dried blood and saliva during asymptomatic and symptomatic SARS-CoV-2 infection**

Abstract

The COVID-19 pandemic continues to have an unprecedented impact on societies and economies worldwide. There remains an ongoing need for high-performance SARS-CoV-2 tests which may be broadly deployed for infection monitoring. Here a highly sensitive single molecule array (Simoa) immunoassay was repi\orted in development for detection of SARS-CoV-2 nucleocapsid protein (N-protein) in venous and capillary blood and saliva. In all matrices in the studies conducted to date we observe >98% negative percent agreement and >90% positive percent agreement with molecular testing for days 1–7 in symptomatic, asymptomatic, and pre-symptomatic PCR+ individuals. N-protein load decreases as anti-SARS-CoV-2 spike-IgG increases, and N-protein levels correlate with RT-PCR Ct-values in saliva, and between matched saliva and capillary blood samples. This Simoa SARS-CoV-2 N-protein assay effectively detects SARS-CoV-2 infection via measurement of antigen levels in blood or saliva, using non-invasive, swab-independent collection methods, offering potential for at home and point of care sample collection.

Reference

https://www.nature.com/articles/s41467-021-22072-9

Potential anti-COVID-19 agents, Cepharanthine and Nelfinavir, and their usage for combination treatment

Abstract

Antiviral treatments targeting the coronavirus disease 2019 are urgently required. We screened a panel of already-approved drugs in a cell culture model of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) and identified two new agents having higher antiviral potentials than the drug candidates such as Remdesivir and Chroloquine in VeroE6/TMPRSS2 cells: the anti-inflammatory drug Cepharanthine and HIV protease inhibitor Nelfinavir. Cepharanthine inhibited SARS-CoV-2 entry through the blocking of viral binding to target cells, whilst Nelfinavir suppressed viral replication partly by protease inhibition. Consistent with their different modes of action, synergistic effect of this combined treatment to limit SARS-CoV-2 proliferation was highlighted. Mathematical modeling *in vitro* antiviral activity coupled with the calculated total drug concentrations in the lung predicts that Nelfinavir will shorten the period until viral clearance by 4.9-days and the combining Cepharanthine/Nelfinavir enhanced their predicted efficacy. These results warrant further evaluation of the potential anti-SARS-CoV-2 activity of Cepharanthine and Nelfinavir.

Reference

https://www.cell.com/iscience/fulltext/S2589-0042(21)00335-7

Sensitivity of infectious SARS-CoV-2 B.1.1.7 and B.1.351 variants to neutralizing antibodies

Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) B.1.1.7 and B.1.351 variants were first identified in the United Kingdom and South Africa, respectively, and have since spread to many countries. These variants harboring diverse mutations in the gene encoding the spike protein raise important concerns about their immune evasion potential. Here, infectious B.1.1.7 and B.1.351 strains were isolated from acutely infected individuals. It was examined that sensitivity of the two variants to SARS-CoV-2 antibodies present in sera and nasal swabs from individuals infected with previously circulating strains or who were recently vaccinated, in comparison with a D614G reference virus. A new rapid neutralization assay was utilized, based on reporter cells

that become positive for GFP after overnight infection. Sera from 58 convalescent individuals collected up to 9 months after symptoms, similarly neutralized B.1.1.7 and D614G. In contrast, after 9 months, convalescent sera had a mean sixfold reduction in neutralizing titers, and 40% of the samples lacked any activity against B.1.351. Sera from 19 individuals vaccinated twice with Pfizer Cominarty, longitudinally tested up to 6 weeks after vaccination, were similarly potent against B.1.1.7 but less efficacious against B.1.351, when compared to D614G. Neutralizing titers increased after the second vaccine dose, but remained 14-fold lower against B.1.351. In contrast, sera from convalescent or vaccinated individuals similarly bound the three spike proteins in a flow cytometry-based serological assay. Neutralizing antibodies were rarely detected in nasal swabs from vaccinees. Thus, faster-spreading SARS-CoV-2 variants acquired a partial resistance to neutralizing antibodies generated by natural infection or vaccination, which was most frequently detected in individuals with low antibody levels. Our results indicate that B1.351, but not B.1.1.7, may increase the risk of infection in immunized individuals.

Reference

https://www.nature.com/articles/s41591-021-01318-5

Lockdowns result in changes in human mobility which may impact the epidemiologic dynamics of SARS-CoV-2

Abstract

In response to the SARS-CoV-2 pandemic, unprecedented travel restrictions and stay-at-home orders were enacted around the world. Ultimately, the public's response to announcements of lockdowns—defined as restrictions on both local movement or long distance travel—will determine how effective these kinds of interventions are. Here, we evaluate the effects of lockdowns on human mobility and simulate how these changes may affect epidemic spread by analyzing aggregated mobility data from mobile phones. We show that in 2020 following lockdown announcements but prior to their implementation, both local and long distance movement increased in multiple locations, and urban-to-rural migration was observed around the world. To examine how these behavioral responses to lockdown policies may contribute to epidemic spread, we developed a simple agent-based spatial model. The model shows that this increased

movement has the potential to increase seeding of the epidemic in less urban areas, which could undermine the goal of the lockdown in preventing disease spread. Lockdowns play a key role in reducing contacts and controlling outbreaks, but appropriate messaging surrounding their announcement and careful evaluation of changes in mobility are needed to mitigate the possible unintended consequences.

Reference

https://www.nature.com/articles/s41598-021-86297-w

Publication Date: Mar 25, 2021

Bispecific IgG neutralizes SARS-CoV-2 variants and prevents escape in mice

Abstract

Neutralizing antibodies targeting the receptor binding domain (RBD) of the SARS-CoV-2 Spike (S) are among the most promising approaches against coronavirus disease 2019 (COVID-19). A bispecific, IgG1-like molecule (CoV-X2) was developed based on two antibodies derived from COVID-19 convalescent donors, C121 and C135. CoV-X2 simultaneously binds two independent sites on the RBD and, unlike its parental antibodies, prevents detectable S binding to Angiotensin-Converting Enzyme 2 (ACE2), the virus cellular receptor. Furthermore, CoV-X2 neutralizes SARS-CoV-2 and its variants of concern, as well as the escape mutants generated by the parental monoclonals. In a novel animal model of SARS-CoV-2 infection with lung inflammation, CoV-X2 protects mice from disease and suppresses viral escape. Thus, simultaneous targeting of non-overlapping RBD epitopes by IgG-like bispecific antibodies is feasible and effective, combining into a single molecule the advantages of antibody cocktails.

Reference

https://www.nature.com/articles/s41586-021-03461-y

In silico investigation of critical binding pattern in SARS-CoV-2 spike protein with angiotensin-converting enzyme 2

Abstract

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is a newly-discovered coronavirus and responsible for the spread of coronavirus disease 2019 (COVID-19). SARS-CoV-2 infected millions of people in the world and immediately became a pandemic in March 2020. SARS-CoV-2 belongs to the *beta*-coronavirus genus of the large family of Coronaviridae. It is now known that its surface spike glycoprotein binds to the angiotensin-converting enzyme-2 (ACE2), which is expressed on the lung epithelial cells, mediates the fusion of the cellular and viral membranes, and facilitates the entry of viral genome to the host cell. Therefore, blocking the virus-cell interaction could be a potential target for the prevention of viral infection. The binding of SARS-CoV-2 to ACE2 is a protein–protein interaction, and so, analyzing the structure of the spike glycoprotein of SARS-CoV-2 and its underlying mechanism to bind the host cell receptor would be useful for the management and treatment of COVID-19. In this study, comparative *in silico* studies were performed to deeply understand the structural and functional details of the interaction between the spike glycoprotein of SARS-CoV-2 and its cognate cellular receptor ACE2. According to the results, the affinity of the ACE2 receptor for SARS-CoV-2 was higher than SARS-CoV. According to the free energy decomposition of the spike glycoprotein-ACE2 complex, we found critical points in three areas which are responsible for the increased binding affinity of SARS-CoV-2 compared with SARS-CoV. These mutations occurred at the receptor-binding domain of the spike glycoprotein that play an essential role in the increasing the affinity of coronavirus to ACE2. For instance, mutations Pro462Ala and Leu472Phe resulted in the altered binding energy from − 2 kcal mol−1 in SARS-COV to − 6 kcal mol−1 in SARS-COV-2. The results demonstrated that some mutations in the receptor-binding motif could be considered as a hot-point for designing potential drugs to inhibit the interaction between the spike glycoprotein and ACE2.

Reference

https://www.nature.com/articles/s41598-021-86380-2

AI-assisted tracking of worldwide non-pharmaceutical interventions for COVID-19

Abstract

Coronavirus disease 2019 (COVID-19) global pandemic has transformed almost every facet of human society throughout the world. Against an emerging, highly transmissible disease, governments worldwide have implemented non-pharmaceutical interventions (NPIs) to slow the spread of the virus. Examples of such interventions include community actions, such as school closures or restrictions on mass gatherings, individual actions including mask wearing and self-quarantine, and environmental actions such as cleaning public facilities. The Worldwide Non-pharmaceutical Interventions Tracker was presented for COVID-19 (WNTRAC), a comprehensive dataset consisting of over 6,000 NPIs implemented worldwide since the start of the pandemic. WNTRAC covers NPIs implemented across 261 countries and territories, and classifies NPIs into a taxonomy of 16 NPI types. NPIs are automatically extracted daily from Wikipedia articles using natural language processing techniques and then manually validated to ensure accuracy and veracity. It was hoped that the dataset will prove valuable for policymakers, public health leaders, and researchers in modeling and analysis efforts to control the spread of COVID-19.

Reference

https://www.nature.com/articles/s41597-021-00878-y

The effect of SARS-CoV-2 D614G mutation on BNT162b2 vaccine-elicited neutralization

Abstract

Initial COVID-19 vaccine candidates were based on the original sequence of SARS-CoV-2. However, the virus has since accumulated mutations, among which the spike D614G is dominant in circulating virus, raising questions about potential virus escape from vaccine-elicited immunity. Here, it was reported that the D614G mutation modestly reduced (1.7–2.4-fold) SARS-CoV-2 neutralization by BNT162b2 vaccine-elicited mouse, rhesus, and human sera, concurring with the 95% vaccine efficacy observed in clinical trial.

Reference

https://www.nature.com/articles/s41541-021-00313-8

SARS-CoV-2 infection rewires host cell metabolism and is potentially susceptible to mTORC1 inhibition

Abstract

Viruses hijack host cell metabolism to acquire the building blocks required for replication. Understanding how SARS-CoV-2 alters host cell metabolism may lead to potential treatments for COVID-19. Here we profile metabolic changes conferred by SARS-CoV-2 infection in kidney epithelial cells and lung air-liquid interface (ALI) cultures, and show that SARS-CoV-2 infection increases glucose carbon entry into the TCA cycle via increased pyruvate carboxylase expression. SARS-CoV-2 also reduces oxidative glutamine metabolism while maintaining reductive carboxylation. Consistent with these changes, SARS-CoV-2 infection increases the activity of mTORC1 in cell lines and lung ALI cultures. Lastly, we show evidence of mTORC1 activation in COVID-19 patient lung tissue, and that mTORC1 inhibitors reduce viral replication in kidney epithelial cells and lung ALI cultures. The results suggested that targeting mTORC1 may be a feasible treatment strategy for COVID-19 patients, although further studies are required to determine the mechanism of inhibition and potential efficacy in patients.

Reference

https://www.nature.com/articles/s41467-021-22166-4

Engineering luminescent biosensors for point-of-care SARS-CoV-2 antibody detection

Abstract

Current serology tests for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antibodies mainly take the form of enzyme-linked immunosorbent assays, chemiluminescent microparticle immunoassays or lateral flow assays, which are either laborious, expensive or lacking sufficient sensitivity and scalability. Here it was presented that the development and validation of a rapid, low-cost, solution-based assay to detect antibodies in serum, plasma, whole blood and to a lesser extent saliva, using rationally designed split luciferase antibody biosensors. This new assay, which

generates quantitative results in 30 min, substantially reduces the complexity and improves the scalability of coronavirus disease 2019 (COVID-19) antibody tests. This assay is well-suited for point-of-care, broad population testing, and applications in low-resource settings, for monitoring host humoral responses to vaccination or viral infection.

Reference

https://www.nature.com/articles/s41587-021-00878-8

Symptoms and syndromes associated with SARS-CoV-2 infection and severity in pregnant women from two community cohorts

Abstract

It was tested whether pregnant and non-pregnant women differ in COVID-19 symptom profile and severity, and we extended previous investigations on hospitalized pregnant women to those who did not require hospitalization. Two female community-based cohorts (18–44 years) provided longitudinal (smartphone application, N = 1,170,315, n = 79 pregnant tested positive) and cross-sectional (web-based survey, N = 1,344,966, n = 134 pregnant tested positive) data, prospectively collected through self-participatory citizen surveillance in UK, Sweden and USA. Pregnant and non-pregnant were compared for frequencies of events, including SARS-CoV-2 testing, symptoms and hospitalization rates. Multivariable regression was used to investigate symptoms severity and comorbidity effects. Pregnant and non-pregnant women positive for SARS-CoV-2 infection were not different in syndromic severity, except for gastrointestinal symptoms. Pregnant were more likely to have received testing, despite reporting fewer symptoms. Pre-existing lung disease was most closely associated with syndromic severity in pregnant hospitalized. Heart and kidney diseases and diabetes increased risk. The most frequent symptoms among non-hospitalized women were anosmia [63% pregnant, 92% non-pregnant] and headache [72%, 62%]. Cardiopulmonary symptoms, including persistent cough [80%] and chest pain [73%], were more frequent among pregnant who were hospitalized. Consistent with observations in non-pregnant populations, lung disease and diabetes were associated with increased risk of more severe SARS-CoV-2 infection during pregnancy.

Reference

https://www.nature.com/articles/s41598-021-86452-3

Stochastic modelling of the effects of human-mobility restriction and viral infection characteristics on the spread of COVID-19

Abstract

After several months of "lockdown" as the sole answer to the COVID-19 pandemic, balancing the re-opening of society against the implementation of non-pharmaceutical measures needed for minimizing interpersonal contacts has become important. Here, a stochastic model was presented that examines this problem. In our model, people are allowed to move between discrete positions on a one-dimensional grid with viral infection possible when two people are collocated at the same site. The model features three sets of adjustable parameters, which characterize (i) viral transmission, (ii) viral detection, and (iii) degree of personal mobility, and as such, it is able to provide a qualitative assessment of the potential for second-wave infection outbreaks based on the timing, extent, and pattern of the lockdown relaxation strategies. The results suggest that a full lockdown will yield the lowest number of infections (as anticipated) but we also found that when personal mobility exceeded a critical level, infections increased, quickly reaching a plateau that depended solely on the population density. Confinement was not effective if not accompanied by a detection/quarantine capacity surpassing 40% of the symptomatic patients. Finally, taking action to ensure a viral transmission probability of less than 0.4, which, in real life, may mean actions such as social distancing or mask-wearing, could be as effective as a soft lockdown.

Reference

https://www.nature.com/articles/s41598-021-86027-2

Immune memory in convalescent patients with asymptomatic or mild COVID-19

Abstract

It is important to evaluate the durability of the protective immune response elicited by primary infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Here, we systematically evaluated the SARS-CoV-2-specific memory B cell and T cell responses in healthy controls and individuals recovered from asymptomatic or

symptomatic infection approximately 6 months prior. Comparatively low frequencies of memory B cells specific for the receptor-binding domain (RBD) of spike glycoprotein (S) persisted in the peripheral blood of individuals who recovered from infection (median 0.62%, interquartile range 0.48-0.69). The SARS-CoV-2 RBD-specific memory B cell response was detected in 2 of 13 individuals who recovered from asymptomatic infection and 10 of 20 individuals who recovered from symptomatic infection. T cell responses induced by S, membrane (M), and nucleocapsid (N) peptide libraries from SARS-CoV-2 were observed in individuals recovered from coronavirus disease 2019 (COVID-19), and cross-reactive T cell responses to SARS-CoV-2 were also detected in healthy controls.

Reference

https://www.nature.com/articles/s41421-021-00250-9

SARS-CoV-2 infection of the oral cavity and saliva

Abstract

Despite signs of infection—including taste loss, dry mouth and mucosal lesions such as ulcerations, enanthema and macules—the involvement of the oral cavity in coronavirus disease 2019 (COVID-19) is poorly understood. To address this, we generated and analyzed two single-cell RNA sequencing datasets of the human minor salivary glands and gingiva (9 samples, 13,824 cells), identifying 50 cell clusters. Using integrated cell normalization and annotation, we classified 34 unique cell subpopulations between glands and gingiva. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) viral entry factors such as ACE2 and TMPRSS members were broadly enriched in epithelial cells of the glands and oral mucosae. Using orthogonal RNA and protein expression assessments, SARS-CoV-2 infection was confirmed in the glands and mucosae. Saliva from SARS-CoV-2-infected individuals harbored epithelial cells exhibiting ACE2 and TMPRSS expression and sustained SARS-CoV-2 infection. Acellular and cellular salivary fractions from asymptomatic individuals were found to transmit SARS-CoV-2 ex vivo. Matched nasopharyngeal and saliva samples displayed distinct viral shedding dynamics, and salivary viral burden correlated with COVID-19 symptoms, including taste loss. Upon recovery, this asymptomatic cohort exhibited sustained salivary IgG antibodies against SARS-CoV-2. Collectively, these data show

that the oral cavity is an important site for SARS-CoV-2 infection and implicate saliva as a potential route of SARS-CoV-2 transmission.

Reference

https://www.nature.com/articles/s41591-021-01296-8

Assessing transmissibility of SARS-CoV-2 lineage B.1.1.7 in England

Abstract

The SARS-CoV-2 lineage B.1.1.7, designated a Variant of Concern 202012/01 (VOC) by Public Health England1, originated in the UK in late Summer to early Autumn 20202. Whole genome SARS-CoV-2 sequence data collected from community-based diagnostic testing shows an unprecedentedly rapid expansion of the B.1.1.7 lineage during Autumn 2020, suggesting a selective advantage. We find that changes in VOC frequency inferred from genetic data correspond closely to changes inferred by S-gene target failures (SGTF) in community-based diagnostic PCR testing. Analysis of trends in SGTF and non-SGTF case numbers in local areas across England shows that the VOC has higher transmissibility than non-VOC lineages, even if the VOC has a different latent period or generation time. The SGTF data indicate a transient shift in the age composition of reported cases, with a larger share of under 20 year olds among reported VOC than non-VOC cases. Time-varying reproduction numbers for the VOC and cocirculating lineages were estimated using SGTF and genomic data. The best supported models did not indicate a substantial difference in VOC transmissibility among different age groups. There is a consensus among all analyses that the VOC has a substantial transmission advantage with a 50% to 100% higher reproduction number.

Reference

https://www.nature.com/articles/s41586-021-03470-x

CORRESPONDANCE

Publication Date: Mar 26, 2021

The emerging plasticity of SARS-CoV-2

Viruses evolve as a result of mutation (misincorporations, insertions or deletions, and recombination) and natural selection for favorable traits such as more efficient viral replication, transmission, and evasion of host defenses. Newly selected traits may be linked in unpredictable ways and raise concern that virus spread and evolution could result in greater virulence (disease severity). The limited diversity of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) reported during 2020, ascribed to the 3′-5′ exonuclease proofreading function of nonstructural protein 14 (nsp14), led to the view that vaccines based on a single sequence of the viral spike (S) protein, which mediates host cell entry, would likely generate immune protection to all circulating variants. However, variants of SARS-CoV-2 with mutations in S have emerged around the world, posing potential challenges for vaccination and antibody-based therapies. The continued spread of SARS-CoV-2 creates the opportunity for accumulation of additional consequential mutations in S and throughout the viral genome.

Although SARS-CoV-2 shares high sequence homology with SARS-CoV, which caused the 2002–2004 SARS outbreak, the coronavirus family is diverse in both sequence and in host receptor preference. For example, SARS-CoV-2 and a “common cold” human coronavirus, HCoV-NL63, both recognize angiotensin-converting enzyme 2 (ACE2) as the host cell receptor, but SARS-CoV-2 and HCoV-NL63 belong to different coronavirus genera and have major sequence and structural differences in the receptor-binding domain (RBD) of S, sharing <30% sequence homology (2). This diversity in S indicates that coronaviruses have broad potential to tolerate changes in both sequence and structure without substantial loss of function. This may partially explain why coronaviruses can undergo zoonotic transmission and suggests that the full evolutionary potential of SARS-CoV-2 has yet to be revealed. The S protein comprises two subunits: S1, which contains the RBD, and S2, which mediates virus–host cell fusion. Antibody-neutralizing epitopes are scattered throughout S but are mostly concentrated within the RBD. Despite the potential for plasticity, after nearly a year of

spread (from December 2019) to >100 million people, there was limited evidence for evolution of SARS-CoV-2 S. The only notable evolutionary event was the D614G (Asp614→Gly) substitution in S1, which increases ACE2 affinity, leading to higher infectivity and transmissibility. Viral sequences deposited in public databases were mostly obtained from the upper respiratory tract during acute infection, before major immune responses have occurred. Such sequences might not capture the effect of within-host immune selection on viral diversification. For more details, read the link given below.

Reference

https://science.sciencemag.org/content/371/6536/1306

COMMENT

Publication Date: Mar 31, 2021

COVID-19 vaccines for patients with haematological conditions

Patients with haematological conditions have been disproportionately affected by the COVID-19 pandemic. A pooled meta-analysis of 3377 predominantly hospitalised patients with haematological malignancies and COVID-19 reported a mortality rate of 34% (95% CI 28–39). Advanced age (≥60 years) and non-White race were identified as risk factors for death. Mortality rate varied on the basis of the type of malignancy: 53% of patients with acquired bone marrow failure syndromes, 41% of patients with acute leukaemias, 32% of patients with lymphomas, 31% of patients with chronic lymphocytic leukaemia, and 34% of patients with myeloproliferative neoplasms. To place these data in perspective, the mean 30-day rate of mortality or referral to hospice was 11·8% (SD 2·5%) in a cohort study of 38 517 adults admitted to hospital with COVID-19 in the USA. The trajectory of COVID-19 in patients with benign haematological conditions such as haemoglobinopathy, haemophilia, pre-existing arterial or venous thromboembolism, and autoimmune cytopenia is relatively unknown, but as in the general population, is influenced by age and comorbidities. Authorised COVID-19 vaccines are safe and effective in the general population. Given the high case fatality rate among patients with haematological conditions, prioritisation of COVID-19 vaccines for this group might appear straightforward. However, common to these vaccines is the exclusion of immunocompromised people from landmark phase 3 randomised controlled trials. Relevant exclusion criteria included the use of immunosuppressive or immunomodulatory agents, immunoglobulin or blood products, asplenia, and autoimmune conditions such as immune thrombocytopenic purpura. Most patients with haematological conditions, therefore, would have been ineligible for these trials. Until COVID-19 vaccines have been rigorously studied in this group, one must examine available data on the immune response to COVID-19 infection and non-COVID-19 vaccines to inform clinical practice and expectations. For more details, read the link given below.

Reference

https://www.thelancet.com/journals/lanhae/article/PIIS2352-3026(21)00073-9/fulltext

REPORT

Publication Date: Mar 25, 2021

mRNA vaccination boosts cross-variant neutralizing antibodies elicited by SARS-CoV-2 infection

Abstract

Emerging SARS-CoV-2 variants have raised concerns about resistance to neutralizing antibodies elicited by previous infection or vaccination. It was examined whether sera from recovered and naïve donors collected prior to, and following immunizations with existing mRNA vaccines, could neutralize the Wuhan-Hu-1 and B.1.351 variants. Pre-vaccination sera from recovered donors neutralized Wuhan-Hu-1 and sporadically neutralized B.1.351, but a single immunization boosted neutralizing titers against all variants and SARS-CoV-1 by up to 1000-fold. Neutralization was due to antibodies targeting the receptor binding domain and was not boosted by a second immunization. Immunization of naïve donors also elicited cross-neutralizing responses, but at lower titers. Our study highlights the importance of vaccinating both uninfected and previously infected persons to elicit cross-variant neutralizing antibodies.

Reference

https://science.sciencemag.org/content/early/2021/03/24/science.abg9175Reference

OPINION

Publication Date: Mar 25, 2021

SARS-CoV-2: Cross-scale insights from ecology and evolution

Abstract

Ecological and evolutionary processes govern the fitness, propagation, and interactions of organisms through space and time, and viruses are no exception. While COVID-19 research has primarily emphasized virological, clinical, and epidemiological perspectives, crucial aspects of the pandemic are fundamentally ecological or evolutionary. Here, we highlight five conceptual domains of ecology and evolution – invasion, consumer-resource interactions, spatial ecology, diversity, and adaptation – that illuminate (sometimes unexpectedly) the emergence and spread of SARS-CoV-2. We describe the applications of these concepts across levels of biological organization and spatial scales, including within individual hosts, host populations, and multi-species communities. Together, these perspectives illustrate the integrative power of ecological and evolutionary ideas and highlight the benefits of interdisciplinary thinking for understanding emerging viruses.

Reference

https://www.cell.com/trends/microbiology/fulltext/S0966-842X(21)00072-X

NEWSLETTER

Publication Date: Mar 30, 2021

COVID research updates: New coronavirus variants spur multi-talented antibody response

New coronavirus variants spur multi-talented antibody response (Mar 30, 2021):

Antibodies from people infected with the 501Y.V2 coronavirus variant first identified in South Africa are also effective against previously circulating variants, suggesting that vaccines against 501Y.V2 might work against a range of coronavirus variants. South Africa's first wave of coronavirus infections peaked in July 2020. The second wave peaked in January 2021, and was driven by the recently discovered 501Y.V2 variant (also called B.1.351). The variant is partially resistant to antibodies against previously circulating variants, raising concerns about the effectiveness of current vaccines against it. Tulio de Oliveira at the University of KwaZulu-Natal in Durban, South Africa, Alex Sigal at the Africa Health Research Institute, also in Durban, and their colleagues tested blood plasma from people in South Africa who had been infected during one of the two waves (S. Cele et al. Nature https://doi.org/f362; 2021). The team found that plasma from the second wave was 15 times more effective at preventing the 501Y.V2 variant from infecting cells in a laboratory dish, compared with plasma from the first wave. The scientists also found that second-wave plasma could neutralize first-wave variants with an effectiveness similar to that of the Pfizer–BioNTech vaccine. This implies that updated vaccines against 501Y.V2 could also protect against earlier coronavirus variants.

'Real-world' study finds vaccines sharply cut infection risk (Mar 30, 2021):

A full vaccination reduces risk of coronavirus infection by roughly 90%, according to a study of US nurses, firefighters and other front-line workers who received an mRNA-based vaccine. Clinical trials have shown that the mRNA-based vaccines made by Moderna and Pfizer–BioNTech are highly effective at protecting people from illness caused by SARS-CoV-2. To learn whether the vaccines also shield people from becoming infected in the first place, Mark Thompson at the US Centers for Disease Control and Prevention in Atlanta, Georgia, and his colleagues studied SARS-CoV-2

test results from nearly 4,000 people whose work puts them at high risk of infection (M. G. Thompson et al. Morb. Mortal. Wkly Rep. https://doi.org/f36s; 2021). Study participants were vaccinated between mid-December 2020 and mid-March 2021. After vaccination, they swabbed their own noses for viral testing once a week for 13 weeks. Participants were considered fully immunized two weeks after receiving their second dose of vaccine. Full immunization was 90% effective at protecting people against infection, and a single dose was 80% effective. But the researchers caution that because very few participants became infected after vaccination, it's difficult to state the vaccines' effectiveness against infection with high precision.

Coronavirus antibodies last for months (Mar 25, 2021):

The neutralizing antibodies that the immune system produces to disable the virus SARS-CoV-2 can last for at least nine months after infection, but not everyone makes them in detectable quantities. Chen Wang at Peking Union Medical College in Beijing and his colleagues took blood samples from more than 9,500 people in some 3,500 randomly selected households in Wuhan, China, the first place known to be widely affected by COVID-19 (Z. He et al. Lancet 397, 1075–1084; 2021). The team took samples at three separate times over the course of 2020: once in April, after the city's lockdown lifted; once in June; and again between October and December. The team tested the samples for antibodies against SARS-CoV-2, which indicate that a person has been infected with the virus. The researchers found that only 7% of the population had been infected with the virus, of whom more than 80% had had no symptoms. Around 40% of the infected people produced neutralizing antibodies that could be detected for the entire study period. The researchers conclude that most people in Wuhan are still susceptible to SARS-CoV-2 infection, and that a mass vaccination campaign is needed to achieve herd immunity.

Reference

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