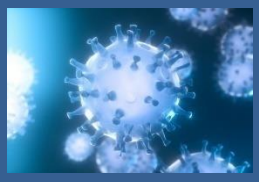
COVID-19

Feb 25 – Mar 03, 2021



RESEARCH PUBLICATIONS

Publication Date: Mar 03, 2021

A multiplexed, next generation sequencing platform for high-throughput detection of SARS-CoV-2

Abstract

Population scale sweeps of viral pathogens, such as SARS-CoV-2, require high intensity testing for effective management. Here, “Systematic Parallel Analysis of RNA coupled to Sequencing for Covid-19 screening” (C19-SPAR-Seq) was described, a multiplexed, scalable, readily automated platform for SARS-CoV-2 detection that is capable of analyzing tens of thousands of patient samples in a single run. To address strict requirements for control of assay parameters and output demanded by clinical diagnostics, we employ a control-based Precision-Recall and Receiver Operator Characteristics (coPR) analysis to assign run-specific quality control metrics. C19-SPAR-Seq coupled to coPR on a trial cohort of several hundred patients performs with a specificity of 100% and sensitivity of 91% on samples with low viral loads, and a sensitivity of >95% on high viral loads associated with disease onset and peak transmissibility. This study establishes the feasibility of employing C19-SPAR-Seq for the large-scale monitoring of SARS-CoV-2 and other pathogens.

Reference

https://www.nature.com/articles/s41467-021-21653-y

Estimated transmissibility and impact of SARS-CoV-2 lineage B.1.1.7 in England

Abstract

A novel SARS-CoV-2 variant, VOC 202012/01 (lineage B.1.1.7), emerged in southeast England in November 2020 and is rapidly spreading toward fixation. Using a variety of

statistical and dynamic modelling approaches, we estimate that this variant has a 43–90% (range of 95% credible intervals 38–130%) higher reproduction number than preexisting variants. A fitted two-strain dynamic transmission model shows that VOC 202012/01 will lead to large resurgences of COVID-19 cases. Without stringent control measures, including limited closure of educational institutions and a greatly accelerated vaccine roll-out, COVID-19 hospitalisations and deaths across England in 2021 will exceed those in 2020. Concerningly, VOC 202012/01 has spread globally and exhibits a similar transmission increase (59–74%) in Denmark, Switzerland, and the United States.

Reference

https://science.sciencemag.org/content/early/2021/03/03/science.abg3055

Quantitative evaluation of SARS-CoV-2 inactivation using a deep ultraviolet light-emitting diode

Abstract

Inactivation technology for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is certainly a critical measure to mitigate the spread of coronavirus disease 2019 (COVID-19). A deep ultraviolet light-emitting diode (DUV-LED) would be a promising candidate to inactivate SARS-CoV-2, based on the well-known antiviral effects of DUV on microorganisms and viruses. However, due to variations in the inactivation effects across different viruses, quantitative evaluations of the inactivation profile of SARS-CoV-2 by DUV-LED irradiation need to be performed. In the present study, we quantify the irradiation dose of DUV-LED necessary to inactivate SARS-CoV-2. For this purpose, we determined the culture media suitable for the irradiation of SARS-CoV-2 and optimized the irradiation apparatus using commercially available DUV-LEDs that operate at a center wavelength of 265, 280, or 300 nm. Under these conditions, we successfully analyzed the relationship between SARS-CoV-2 infectivity and the irradiation dose of the DUV-LEDs at each wavelength without irrelevant biological effects. In conclusion, total doses of 1.8 mJ/cm^2 for 265 nm, 3.0 mJ/cm^2 for 280 nm, and 23 mJ/cm^2 for 300 nm are required to inactivate 99.9% of SARS-CoV-2. Our results provide quantitative antiviral effects of DUV irradiation on SARS-CoV-2, serving as basic knowledge of inactivation technologies against SARS-CoV-2.

Reference

https://www.nature.com/articles/s41598-021-84592-0

Immunogenicity of prime-boost protein subunit vaccine strategies against SARS-CoV-2 in mice and macaques

Abstract

SARS-CoV-2 vaccines are advancing into human clinical trials, with emphasis on eliciting high titres of neutralising antibodies against the viral spike (S). However, the merits of broadly targeting S versus focusing antibody onto the smaller receptor binding domain (RBD) are unclear. Here we assess prototypic S and RBD subunit vaccines in homologous or heterologous prime-boost regimens in mice and non-human primates. We find S is highly immunogenic in mice, while the comparatively poor immunogenicity of RBD is associated with limiting germinal centre and T follicular helper cell activity. Boosting S-primed mice with either S or RBD significantly augments neutralising titres, with RBD-focussing driving moderate improvement in serum neutralisation. In contrast, both S and RBD vaccines are comparably immunogenic in macaques, eliciting serological neutralising activity that generally exceed levels in convalescent humans. These studies confirm recombinant S proteins as promising vaccine candidates and highlight multiple pathways to achieving potent serological neutralisation.

Reference

https://www.nature.com/articles/s41467-021-21665-8

Camostat mesylate inhibits SARS-CoV-2 activation by TMPRSS2-related proteases and its metabolite GBPA exerts antiviral activity

Abstract

Background: Antivirals are needed to combat the COVID-19 pandemic, which is caused by SARS-CoV-2. The clinically-proven protease inhibitor Camostat mesylate inhibits SARS-CoV-2 infection by blocking the virus-activating host cell protease TMPRSS2. However, antiviral activity of Camostat mesylate metabolites and potential viral resistance have not been analyzed. Moreover, antiviral activity of Camostat mesylate in human lung tissue remains to be demonstrated.

Methods: Recombinant TMPRSS2, reporter particles bearing the spike protein of SARS-CoV-2 or authentic SARS-CoV-2 was used to assess inhibition of TMPRSS2 and viral entry, respectively, by Camostat mesylate and its metabolite GBPA.

Findings: It was shown that several TMPRSS2-related proteases activate SARS-CoV-2 and that two, TMPRSS11D and TMPRSS13, are robustly expressed in the upper respiratory tract. However, entry mediated by these proteases was blocked by Camostat mesylate. The Camostat metabolite GBPA inhibited recombinant TMPRSS2 with reduced efficiency as compared to Camostat mesylate. In contrast, both inhibitors exhibited similar antiviral activity and this correlated with the rapid conversion of Camostat mesylate into GBPA in the presence of serum. Finally, Camostat mesylate and GBPA blocked SARS-CoV-2 spread in human lung tissue ex vivo and the related protease inhibitor Nafamostat mesylate exerted augmented antiviral activity.

Interpretation: The results suggested that SARS-CoV-2 can use TMPRSS2 and closely related proteases for spread in the upper respiratory tract and that spread in the human lung can be blocked by Camostat mesylate and its metabolite GBPA.

Reference

https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(21)00048-7/fulltext

Non-steroidal anti-inflammatory agent use may not be associated with mortality of coronavirus disease 19

Abstract

Non-steroidal anti-inflammatory drugs (NSAIDs) have been widely used in patients with respiratory infection, but their safety in coronavirus disease 19 (Covid-19) patients has not been fully investigated. an association between NSAID use and outcomes of Covid-19, was evaluated. This study was a retrospective observational cohort study based on insurance benefit claims sent to the Health Insurance Review and Assessment Service of Korea by May 15, 2020. These claims comprised all Covid-19-tested cases and history of medical service use for the past 3 years in these patients. The primary outcome was all-cause mortality, and the secondary outcome was need for ventilator care. Among 7590 patients diagnosed with Covid-19, two distinct cohorts were generated based on NSAID or acetaminophen prescription within 2 weeks before

Covid-19 diagnosis. A total of 398 patients was prescribed NSAIDs, and 2365 patients were prescribed acetaminophen. After propensity score matching, 397 pairs of data set were generated, and all-cause mortality of the NSAIDs group showed no significant difference compared with the acetaminophen group (4.0% vs. 3.0%; hazard ratio [HR], 1.33; 95% confidence interval [CI], 0.63–2.88; P = 0.46). The rate of ventilator care also did not show significantly different results between the two groups (2.0% vs. 1.3%; HR, 1.60; 95% CI 0.53–5.30; P = 0.42). Use of NSAIDs was not associated with mortality or ventilator care in Covid-19 patients. NSAIDs may be safely used to relieve symptoms in patients with suspicion of Covid-19.

Reference

https://www.nature.com/articles/s41598-021-84539-5

Association of angiotensin-converting enzyme inhibitors and angiotensin-receptor blockers with risk of mortality, severity or SARS-CoV-2 test positivity in COVID-19 patients: Meta-analysis

Abstract

The effects of angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin II receptor blockers (ARBs) in the treatment of COVID-19 are highly debated. This study was aimed to assess aggregated risk by investigating the association of ACEIs/ARBs users against non-users of ACEIs/ARBs with the risk of mortality or severe clinical manifestations or magnitude of SARS-CoV-2 test positivity in COVID-19 patients. Systematic literature search was carried out in different databases for eligible studies. The pooled relative risks (RRs) were measured using RevMan software where P<0.05 was set as statistical significance. In total, 10 studies were included in this analysis. After pooled estimation, it was demonstrated that SARS-CoV-2 positive patients taking ACEIs/ARBs were not associated with an increased risk of mortality compared to those not taking ACEIs/ARBs (RR 0.89; 95% CI 0.64–1.23; P=0.48). Furthermore, the risk of composite severe clinical manifestations was not significantly different between the positive patients with or without ACEIs/ARBs users (RR 1.29; 95% CI 0.81–2.04; P=0.28). There was no risk difference for SARS-CoV-2 test positivity in patients with or without ACEIs/ARBs users (RR 1.00; 95% CI 0.95–1.05; P=0.91). These findings may

augment current professional society guidelines for not discontinuing ACEIs/ARBs in treating COVID-19 patients where it is clinically indicated.

Reference

https://www.nature.com/articles/s41598-021-84678-9

Clinical evidence of an interferon–glucocorticoid therapeutic synergy in COVID-19

Abstract

Synthetic glucocorticoid dexamethasone is the first trial-proven drug that reduces COVID-19 mortality by suppressing immune system. In contrast, interferons are a crucial component of host antiviral immunity and can be directly suppressed by glucocorticoids. To investigate whether therapeutic interferons can compensate glucocorticoids-induced loss of antiviral immunity, we retrospectively analyzed a cohort of 387 PCR-confirmed COVID-19 patients with quasi-random exposure to interferons and conditional exposure to glucocorticoids. Among patients receiving glucocorticoids, early interferon therapy was associated with earlier hospital discharge (adjusted HR 1.68, 95% CI 1.19–2.37) and symptom relief (adjusted HR 1.48, 95% CI 1.06–2.08), while these associations were insignificant among glucocorticoids nonusers. Early interferon therapy was also associated with lower prevalence of prolonged viral shedding (adjusted OR 0.24, 95% CI 0.10–0.57) only among glucocorticoids users. Additionally, these associations were glucocorticoid cumulative dose- and timing-dependent. These findings reveal potential therapeutic synergy between interferons and glucocorticoids in COVID-19 that warrants further investigation.

Reference

https://www.nature.com/articles/s41392-021-00496-5

A predictive internet-based model for COVID-19 hospitalization census

Abstract

The COVID-19 pandemic has strained hospital resources and necessitated the need for predictive models to forecast patient care demands in order to allow for adequate staffing and resource allocation. Recently, other studies have looked at associations

between Google Trends data and the number of COVID-19 cases. Expanding on this approach, we propose a vector error correction model (VECM) for the number of COVID-19 patients in a healthcare system (Census) that incorporates Google search term activity and healthcare chatbot scores. The VECM provided a good fit to Census and very good forecasting performance as assessed by hypothesis tests and mean absolute percentage prediction error. Although our study and model have limitations, we have conducted a broad and insightful search for candidate Internet variables and employed rigorous statistical methods. We have demonstrated the VECM can potentially be a valuable component to a COVID-19 surveillance program in a healthcare system.

Reference

https://www.nature.com/articles/s41598-021-84091-2

COVID-19: A simple statistical model for predicting intensive care unit load in exponential phases of the disease

Abstract

One major bottleneck in the ongoing COVID-19 pandemic is the limited number of critical care beds. Due to the dynamic development of infections and the time lag between when patients are infected and when a proportion of them enters an intensive care unit (ICU), the need for future intensive care can easily be underestimated. To infer future ICU load from reported infections, a simple statistical model was suggested that accounts for time lags and allows for making predictions depending on different future growth of infections. The model was evaluated for three heavily affected regions in Europe, namely Berlin (Germany), Lombardy (Italy), and Madrid (Spain). Before extensive containment measures made an impact, we first estimate the region-specific model parameters, namely ICU rate, time lag between infection, and ICU admission as well as length of stay in ICU. Whereas for Berlin, an ICU rate of 6%, a time lag of 6 days, and a stay of 12 days in ICU provide the best fit of the data, for Lombardy and Madrid the ICU rate was higher (18% and 15%) and the time lag (0 and 3 days) and the stay in ICU (3 and 8 days) shorter. The region-specific models are then used to predict future ICU load assuming either a continued exponential phase with varying growth rates (0–15%) or linear growth. By keeping the growth rates flexible, this model allows

for taking into account the potential effect of diverse containment measures. Thus, the model can help to predict a potential exceedance of ICU capacity depending on future growth. A sensitivity analysis for an extended time period shows that the proposed model is particularly useful for exponential phases of the disease.

Reference

https://www.nature.com/articles/s41598-021-83853-2

The SARS-CoV-2 subgenome landscape and its novel regulatory features

Abstract

COVID-19, caused by Coronavirus SARS-CoV-2, is now in global pandemic. Coronaviruses are known to generate negative subgenomes (sgRNAs) through Transcription-Regulating Sequence (TRS)-dependent template switch, but the global dynamic landscapes of coronaviral subgenomes and regulatory rules remain unclear. Here, using NGS short-read and Nanopore long-read poly(A) RNA sequencing in two cell types at multiple time points post-infection of SARS-CoV-2, hundreds of template switches were identified and constructed the dynamic landscapes of SARS-CoV-2 subgenomes. Interestingly, template switch could occur in bidirectional manner, with diverse SARS-CoV-2 subgenomes generated from successive template switching events. The majority of template switches result from RNA-RNA interactions, including seed and compensatory modes, with terminal pairing status as a key determinant. Moreover, two TRS-independent template switch modes are also responsible for subgenome biogenesis. Collectively, our findings reveal the subgenome landscape of SARS-CoV-2 and its regulatory features, providing a molecular basis for understanding subgenome biogenesis and developing novel anti-viral strategies.

Reference

https://www.cell.com/molecular-cell/fulltext/S1097-2765(21)00166-0

SARS-CoV-2 variant B.1.1.7 is susceptible to neutralizing antibodies elicited by ancestral Spike vaccines

Abstract

All current vaccines for COVID-19 utilize ancestral SARS-CoV-2 Spike with the goal of generating protective neutralizing antibodies. The recent emergence and rapid spread of several SARS-CoV-2 variants carrying multiple Spike mutations raise concerns about possible immune escape. One variant, first identified in the United Kingdom (B.1.1.7, also called 501Y.V1 or 20I), contains eight Spike mutations with potential to impact antibody therapy, vaccine efficacy and risk of reinfection. Here we show that B.1.1.7 remains sensitive to neutralization, albeit at moderately reduced levels (~2-fold), by serum samples from convalescent individuals and recipients of an mRNA vaccine (mRNA-1273, (Moderna) and a protein nanoparticle vaccine (NVX-CoV2373, Novavax). A subset of monoclonal antibodies to the receptor binding domain (RBD) of Spike are less effective against the variant while others are largely unaffected. These findings indicate that variant B.1.1.7 is unlikely to be a major concern for current vaccines or for an increased risk of reinfection.

Reference

https://www.cell.com/cell-host-microbe/fulltext/S1931-3128(21)00102-5

Binding mode of SARS-CoV2 fusion peptide to human cellular membrane

Abstract

Infection of human cells by the SARS-CoV2 relies on its binding to a specific receptor and subsequent fusion of the viral and host cell membranes. The fusion peptide (FP), a short peptide segment in the spike protein, plays a central role in the initial penetration of the virus into the host cell membrane, followed by the fusion of the two membranes. Here, an array of molecular dynamics (MD) simulations were used, taking advantage of the Highly Mobile Membrane Mimetic (HMMM) model, to investigate the interaction of the SARS-CoV2 FP with a lipid bilayer representing mammalian cellular membranes at an atomic level, and to characterize the membrane-bound form of the peptide. Six independent systems were generated by changing the initial positioning and orientation of the FP with respect to the membrane, and each system was simulated in five

independent replicas, each for 300 ns. In 73% of the simulations, the FP reaches a stable, membrane-bound configuration where the peptide deeply penetrated into the membrane. Clustering of the results reveals three major membrane binding modes (binding modes 1-3) where binding mode 1 populates over half of the data points. Taking into account the sequence conservation among the viral FPs and the results of mutagenesis studies establishing the role of specific residues in the helical portion of the FP in membrane association, the significant depth of penetration of the whole peptide, and the dense population of the respective cluster, we propose that the most deeply inserted membrane-bound form (binding mode 1) represents more closely the biologically relevant form. Analysis of FP-lipid interactions shows the involvement of specific residues, previously described as the “fusion active core residues”, in membrane binding. Taken together, the results shed light on a key step involved in SARS-CoV2 infection with potential implications in designing novel inhibitors.

Reference

https://www.cell.com/biophysj/fulltext/S0006-3495(21)00199-5

Publication Date: Mar 02, 2021

ACE2 receptor usage reveals variation in susceptibility to SARS-CoV and SARS-CoV-2 infection among bat species

Abstract

Bats are the suggested natural hosts for severe acute respiratory syndrome coronavirus (SARS-CoV) and the causal agent of the coronavirus disease 2019 (COVID-19) pandemic, SARS-CoV-2. The interaction of viral spike proteins with their host receptor angiotensin-converting enzyme 2 (ACE2) is a critical determinant of potential hosts and cross-species transmission. Here, virus–host receptor binding and infection assays were used to examine 46 ACE2 orthologues from phylogenetically diverse bat species, including those in close and distant contact with humans. We found that 24, 21 and 16 of them failed to support infection by SARS-CoV, SARS-CoV-2 or both viruses, respectively. Furthermore, it was confirmed that infection assays in human cells were consistent with those in two bat cell lines. Additionally, genetic and functional analyses were used to identify critical residues in bat ACE2 receptors associated with viral entry

restrictions. The results suggested that many bat species may not be the potential hosts of one or both viruses and that no correlation was identified between proximity to humans and probability of being natural hosts of SARS-CoV or SARS-CoV-2. This study demonstrates dramatic variation in susceptibility to SARS-CoV and SARS-CoV-2 infection among bat species and adds knowledge towards a better understanding of coronavirus–bat interaction.

Reference

https://www.nature.com/articles/s41559-021-01407-1

Immunogenicity and protective efficacy of inactivated SARS-CoV-2 vaccine candidate, BBV152 in rhesus macaques

Abstract

The COVID-19 pandemic is a global health crisis that poses a great challenge to the public health system of affected countries. Safe and effective vaccines are needed to overcome this crisis. Here, the protective efficacy and immunogenicity of an inactivated SARS-CoV-2 vaccine were developed and assessed in rhesus macaques. Twenty macaques were divided into four groups of five animals each. The group was administered a placebo, while three groups were immunized with three different vaccine candidates of BBV152 at 0 and 14 days. All the macaques were challenged with SARS-CoV-2 fourteen days after the second dose. The protective response was observed with increasing SARS-CoV-2 specific IgG and neutralizing antibody titers from 3rd-week post-immunization. Viral clearance was observed from bronchoalveolar lavage fluid, nasal swab, throat swab and lung tissues at 7 days post-infection in the vaccinated groups. No evidence of pneumonia was observed by histopathological examination in vaccinated groups, unlike the placebo group which exhibited interstitial pneumonia and localization of viral antigen in the alveolar epithelium and macrophages by immunohistochemistry. This vaccine candidate BBV152 has completed Phase I/II (NCT04471519) clinical trials in India and is presently in phase III, data of this study substantiates the immunogenicity and protective efficacy of the vaccine candidates.

Reference

https://www.nature.com/articles/s41467-021-21639-w

Single-cell meta-analysis of SARS-CoV-2 entry genes across tissues and demographics

Abstract

Angiotensin-converting enzyme 2 (ACE2) and accessory proteases (TMPRSS2 and CTSL) are needed for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) cellular entry, and their expression may shed light on viral tropism and impact across the body. The cell-type-specific expression of ACE2, TMPRSS2 and CTSL were assessed across 107 single-cell RNA-sequencing studies from different tissues. ACE2, TMPRSS2 and CTSL are coexpressed in specific subsets of respiratory epithelial cells in the nasal passages, airways and alveoli, and in cells from other organs associated with coronavirus disease 2019 (COVID-19) transmission or pathology. We performed a meta-analysis of 31 lung single-cell RNA-sequencing studies with 1,320,896 cells from 377 nasal, airway and lung parenchyma samples from 228 individuals. This revealed cell-type-specific associations of age, sex and smoking with expression levels of ACE2, TMPRSS2 and CTSL. Expression of entry factors increased with age and in males, including in airway secretory cells and alveolar type 2 cells. Expression programs shared by ACE2+TMPRSS2+ cells in nasal, lung and gut tissues included genes that may mediate viral entry, key immune functions and epithelial–macrophage cross-talk, such as genes involved in the interleukin-6, interleukin-1, tumor necrosis factor and complement pathways. Cell-type-specific expression patterns may contribute to the pathogenesis of COVID-19, and the work highlights putative molecular pathways for therapeutic intervention.

Reference

https://www.nature.com/articles/s41591-020-01227-z

Impact of SARS-CoV-2 on the clinical outcomes and placental pathology of pregnant women and their infants: A systematic review

Abstract

Pregnant women are susceptible to viral infections due to physiological changes such as cell-mediated immunity. No severe adverse pregnancy or neonatal outcomes have been consistently reported in 2019 novel coronavirus disease (COVID-19) positive

pregnancy cases. There are controversies around the role of COVID-19 in pregnancy. A systematic review was conducted to examine clinical maternal and neonatal clinical outcomes. Studies were included if they reported SARS-CoV-2 infection among pregnant women and/or COVID-19 positive neonates as validated by positive antibody testing or viral testing using polymerase chain reaction. Case series, case reports, case-control studies, and comparative studies were included. Eight hundred and thirty-seven records were identified, resulting in 525 records for level I screening. Forty-one were included after full-text review. Results suggest elevated rates of intensive care unit (ICU) admission, gestational diabetes, preeclampsia, C-sections, pre-term birth, and C-reactive protein (CRP) in comparison to pregnant women without SARS-CoV-2. Careful monitoring of pregnancies with SARS-CoV-2 is recommended.

Reference

https://www.cell.com/heliyon/fulltext/S2405-8440(21)00498-9

The prevalence of antibodies to SARS-CoV-2 among blood donors in China

Abstract

In this study, the seroprevalence of SARS-CoV-2 antibodies were investigated among blood donors in the cities of Wuhan, Shenzhen, and Shijiazhuang in China. From January to April 2020, 38,144 healthy blood donors in the three cities were tested for total antibody against SARS-CoV-2 followed by pseudotype SARS-CoV-2 neutralization tests, IgG, and IgM antibody testing. Finally, a total of 398 donors were confirmed positive. The age- and sex-standardized SARS-CoV-2 seroprevalence among 18–60 year-old adults (18–65 year-old in Shenzhen) was 2.66% (95% CI: 2.24%–3.07%) in Wuhan, 0.033% (95% CI: 0.0029%–0.267%) in Shenzhen, and 0.0028% (95% CI: 0.0001%–0.158%) in Shijiazhuang, respectively. Female sex and older-age were identified to be independent risk factors for SARS-CoV-2 seropositivity among blood donors in Wuhan. As most of the population of China remained uninfected during the early wave of the COVID-19 pandemic, effective public health measures are still certainly required to block viral spread before a vaccine is widely available.

Reference

https://www.nature.com/articles/s41467-021-21503-x

SARS2 simplified scores to estimate risk of hospitalization and death among patients with COVID-19

Abstract

Although models have been developed for predicting severity of COVID-19 from the medical history of patients, simplified models with good accuracy could be more practical. In this study, the utility of simpler models were examined for estimating risk of hospitalization of patients with COVID-19 and mortality of these patients based on demographic characteristics (sex, age, race, median household income based on zip code) and smoking status of 12,347 patients who tested positive at Mass General Brigham centers. The corresponding electronic records were queried (02/26–07/14/2020) to construct derivation and validation cohorts. The derivation cohort was used to fit generalized linear models for estimating risk of hospitalization within 30 days of COVID-19 diagnosis and mortality within approximately 3 months for the hospitalized patients. In the validation cohort, the model resulted in c-statistics of 0.77 [95% CI 0.73–0.80] for hospitalization, and 0.84 [95% CI 0.74–0.94] for mortality among hospitalized patients. Higher risk was associated with older age, male sex, Black ethnicity, lower socioeconomic status, and current/past smoking status. The models can be applied to predict the absolute risks of hospitalization and mortality, and could aid in individualizing the decision making when detailed medical history of patients is not readily available.

Reference

https://www.nature.com/articles/s41598-021-84603-0

SARS-CoV-2 501Y.V2 escapes neutralization by South African COVID-19 donor plasma

Abstract

SARS-CoV-2 501Y.V2 (B.1.351), a novel lineage of coronavirus causing COVID-19, contains substitutions in two immunodominant domains of the spike protein. Here, we show that pseudovirus expressing 501Y.V2 spike protein completely escapes three classes of therapeutically relevant antibodies. This pseudovirus also exhibits substantial to complete escape from neutralization, but not binding, by convalescent plasma. These

data highlight the prospect of reinfection with antigenically distinct variants and foreshadows reduced efficacy of spike-based vaccines.

Reference

https://www.nature.com/articles/s41591-021-01285-x

Prognostic value of cardiac biomarkers in COVID-19 infection

Abstract

Multiple Biomarkers have recently been shown to be elevated in COVID-19, a respiratory infection with multi-organ dysfunction; however, information regarding the prognostic value of cardiac biomarkers as it relates to disease severity and cardiac injury are inconsistent. The goal of this meta-analysis was to summarize the evidence regarding the prognostic relevance of cardiac biomarkers from data available in published reports. PubMed, Embase and Web of Science were searched from inception through April 2020 for studies comparing median values of cardiac biomarkers in critically ill versus non-critically ill COVID-19 patients, or patients who died versus those who survived. The weighted mean differences (WMD) and 95% confidence interval (CI) between the groups were calculated for each study and combined using a random effects meta-analysis model. The odds ratio (OR) for mortality based on cardiac injury was combined from studies reporting it. Troponin levels were significantly higher in COVID-19 patients who died or were critically ill versus those who were alive or not critically ill (WMD 0.57, 95% CI 0.43–0.70, $p < 0.001$). Additionally, BNP levels were also significantly higher in patients who died or were critically ill (WMD 0.45, 95% CI − 0.21–0.69, $p < 0.001$). Cardiac injury was independently associated with significantly increased odds of mortality (OR 6.641, 95% CI 1.26–35.1, $p = 0.03$). A significant difference in levels of D-dimer was seen in those who died or were critically ill. CK levels were only significantly higher in those who died versus those who were alive (WMD 0.79, 95% CI 0.25–1.33, $p = 0.004$). Cardiac biomarkers add prognostic value to the determination of the severity of COVID-19 and can predict mortality.

Reference

https://www.nature.com/articles/s41598-021-84643-6

COVID-19 salivary Raman fingerprint: Innovative approach for the detection of current and past SARS-CoV-2 infections

Abstract

The pandemic of COVID-19 is continuously spreading, becoming a worldwide emergency. Early and fast identification of subjects with a current or past infection must be achieved to slow down the epidemiological widening. Here a Raman-based approach was reported for the analysis of saliva, able to significantly discriminate the signal of patients with a current infection by COVID-19 from healthy subjects and/or subjects with a past infection. The results demonstrated the differences in saliva biochemical composition of the three experimental groups, with modifications grouped in specific attributable spectral regions. The Raman-based classification model was able to discriminate the signal collected from COVID-19 patients with accuracy, precision, sensitivity and specificity of more than 95%. In order to translate this discrimination from the signal-level to the patient-level, a Deep Learning model was developed, obtaining accuracy in the range 89–92%. These findings have implications for the creation of a potential Raman-based diagnostic tool, using saliva as minimal invasive and highly informative biofluid, demonstrating the efficacy of the classification model.

Reference

https://www.nature.com/articles/s41598-021-84565-3

Soluble ACE2-mediated cell entry of SARS-CoV-2 via interaction with proteins related to the renin-angiotensin system

Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) can cause acute respiratory disease and multiorgan failure. Finding human host factors that are essential for SARS-CoV-2 infection could facilitate the formulation of treatment strategies. Using a human kidney cell line—HK-2—that is highly susceptible to SARS-CoV-2, a genome-wide RNAi screen was performed and identified virus dependency factors (VDFs), which play regulatory roles in biological pathways linked to clinical manifestations of SARS-CoV-2 infection. A role was found for a secretory form of SARS-CoV-2 receptor, soluble angiotensin converting enzyme 2 (sACE2), in SARS-CoV-2 infection. Further

investigation revealed that SARS-CoV-2 exploits receptor-mediated endocytosis through interaction between its spike with sACE2 or sACE2-vasopressin via AT1 or AVPR1B, respectively. The identification of VDFs and the regulatory effect of sACE2 on SARS-CoV-2 infection shed insight into pathogenesis and cell entry mechanism of SARS-CoV-2 as well as potential treatment strategies for COVID-19.

Reference

https://www.cell.com/cell/fulltext/S0092-8674(21)00283-X

Clinical characteristics and mortality associated with COVID-19 in Jakarta, Indonesia: A hospital-based retrospective cohort study

Abstract

Background: Data on COVID-19-related mortality and associated factors from low-resource settings are scarce. This study examined clinical characteristics and factors associated with in-hospital mortality of COVID-19 patients in Jakarta, Indonesia, from March 2 to July 31, 2020.

Methods: This retrospective cohort included all hospitalised patients with PCR-confirmed COVID-19 in 55 hospitals. A demographic and clinical data was extracted including hospital outcomes (discharge or death). Logistic regression was used to examine factors associated with mortality.

Findings: Of 4265 patients with a definitive outcome by July 31, 3768 (88%) were discharged and 497 (12%) died. The median age was 46 years (IQR 32–57), 5% were children, and 31% had >1 comorbidity. Age-specific mortalities were 11% (7/61) for <5 years; 4% (1/23) for 5–9; 2% (3/133) for 10–19; 2% (8/638) for 20–29; 3% (26/755) for 30–39; 7% (61/819) for 40–49; 17% (155/941) for 50–59; 22% (132/611) for 60–69; and 34% (96/284) for ≥70. Risk of death was associated with higher age, male sex; pre-existing hypertension, diabetes, or chronic kidney disease; clinical diagnosis of pneumonia; multiple (>3) symptoms; immediate ICU admission, or intubation. Across all ages, risk of death was higher for patients with >1 comorbidity compared to those without; notably the risk was six-fold increased among patients <50 years (adjusted odds ratio 5.87, 95%CI 3.28–10.52; 27% vs 3% mortality).

Interpretation: Overall in-hospital mortality was lower than reported in high-income countries, probably due to younger age distribution and fewer comorbidities. Deaths occurred across all ages, with >10% mortality among children <5 years and adults >50 years.

Reference

https://www.thelancet.com/journals/lanwpc/article/PIIS2666-6065(21)00017-1/fulltext

Multi-site assessment of rapid, point-of-care antigen testing for the diagnosis of SARS-CoV-2 infection in a low-prevalence setting: A validation and implementation study

Abstract

Background: In Australia, COVID-19 diagnosis relies on RT-PCR testing which is relatively costly and time-consuming. To date, few studies have assessed the performance and implementation of rapid antigen-based SARS-CoV-2 testing in a setting with a low prevalence of COVID-19 infections, such as Australia.

Methods: This study recruited participants presenting for COVID-19 testing at three Melbourne metropolitan hospitals during a period of low COVID-19 prevalence. The Abbott PanBioTM COVID-19 Ag point-of-care test was performed alongside RT-PCR. In addition, participants with COVID-19 notified to the Victorian Government were invited to provide additional swabs to aid validation. Implementation challenges were also documented.

Findings: The specificity of the Abbott PanBioTM COVID-19 Ag test was 99.96% (95% CI 99.73 - 100%). Sensitivity amongst participants with RT-PCR-confirmed infection was dependent upon the duration of symptoms reported, ranging from 77.3% (duration 1 to 33 days) to 100% in those within seven days of symptom onset. A range of implementation challenges were identified which may inform future COVID-19 testing strategies in a low prevalence setting.

Interpretation: Given the high specificity, antigen-based tests may be most useful in rapidly triaging public health and hospital resources while expediting confirmatory RT-PCR testing. Considering the limitations in test sensitivity and the potential for rapid transmission in susceptible populations, particularly in hospital settings, careful

consideration is required for implementation of antigen testing in a low prevalence setting.

Reference

https://www.thelancet.com/journals/lanwpc/article/PIIS2666-6065(21)00024-9/fulltext

Publication Date: Mar 01, 2021

Lung expression of genes putatively involved in SARS-CoV-2 infection is modulated in cis by germline variants

Abstract

Germline variants in genes involved in SARS-CoV-2 cell entry and in host innate immune responses to viruses may influence the susceptibility to infection. This study used whole-genome analyses of lung tissue to identify polymorphisms acting as expression quantitative trait loci (eQTLs) for 60 genes of relevance to SARS-CoV-2 infection susceptibility. The expression of genes with confirmed or possible roles in viral entry–replication and in host antiviral responses was studied in the non-diseased lung tissue of 408 lung adenocarcinoma patients. No gene was differently expressed by sex, but APOBEC3H levels were higher and PARP12 levels lower in older individuals. A total of 125 cis-eQTLs (false discovery rate < 0.05) was found to modulate mRNA expression of 15 genes (ABO, ANPEP, AP2A2, APOBEC3D, APOBEC3G, BSG, CLEC4G, DDX58, DPP4, FURIN, FYCO1, RAB14, SERINC3, TRIM5, ZCRB1). eQTLs regulating ABO and FYCO1 were found in COVID-19 susceptibility loci. No trans-eQTLs were identified. Genetic control of the expression of these 15 genes, which encode putative virus receptors, proteins required for vesicle trafficking, enzymes that interfere with viral replication, and other restriction factors, may underlie interindividual differences in risk or severity of infection with SARS-CoV-2 or other viruses.

Reference

https://www.nature.com/articles/s41431-021-00831-y

Impact of SARS-CoV-2 infection on the recovery of peripheral blood mononuclear cells by density gradient

Abstract

SARS-CoV-2 virus infection is responsible for coronavirus disease (COVID-19), which is characterised by a hyperinflammatory response that plays a major role in determining the respiratory and immune-mediated complications of this condition. While isolating peripheral blood mononuclear cells (PBMCs) from whole blood of COVID-19 patients by density gradient centrifugation, we noticed some changes in the floating properties and in the sedimentation of the cells on density medium. Investigating this further, we found that in early phase COVID-19 patients, characterised by reduced circulating lymphocytes and monocytes, the PBMC fraction contained surprisingly high levels of neutrophils. Furthermore, the neutrophil population exhibited alterations in the cell size and in the internal complexity, consistent with the presence of low density neutrophils (LDNs) and immature forms, which may explain the shift seen in the floating abilities and that may be predictive of the severity of the disease. The percentage of this subset of neutrophils found in the PBMC band was rather spread (35.4 ± 27.2%, with a median 28.8% and IQR 11.6–56.1, Welch's t-test early phase COVID-19 versus blood donor healthy controls $P < 0.0001$). Results confirm the presence of an increased number of LDNs in patients with early stage COVID-19, which correlates with disease severity and may be recovered by centrifugation on a density gradient together with PBMCs.

Reference

https://www.nature.com/articles/s41598-021-83950-2

Previous viral symptoms and individual mothers influenced the leveled duration of human milk antibodies cross-reactive to S1 and S2 subunits from SARS-CoV-2, HCoV-229E, and HCoV-OC43

Abstract

Objective: The influence of previous viral symptoms on the level and duration of human milk antibodies reactive to SARS-CoV-2, and common human coronaviruses (HCoVs) was investigated.

Study design: Antibodies reactive to S1 and S2 subunits from SARS-CoV-2, HCoV-OC43, and HCoV-229E were measured via ELISA in human milk samples collected from March to June 2020 in mothers with and without viral symptoms.

Results: The presence of viral symptoms influenced the levels of SARS-CoV-2 S2-reactive SIgA/IgA and tended to influence SARS-CoV-2 S1 SIgA/IgA and S2-reactive SIgM/IgM in human milk but did not relate to IgG. HCoV-229E S1 + S2-reactive SIgA/IgA and SIgM/IgM, as well as HCoV-OC43 S1 + S2-reactive IgG were related to the symptoms. The duration of antibody levels in human milk in mothers with viral symptoms varied between 3 and 4 months post maternal report of viral symptoms.

Conclusion: Previous viral symptoms and individual mothers may change the antibody cross-reactive levels to SARS-CoV-2 and HCoVs in human milk.

Reference

https://www.nature.com/articles/s41372-021-01001-0

SARS-CoV-2 engages inflammasome and pyroptosis in human primary monocytes

Abstract

Infection by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been associated with leukopenia and uncontrolled inflammatory response in critically ill patients. A better comprehension of SARS-CoV-2-induced monocyte death is essential for the identification of therapies capable to control the hyper-inflammation and reduce viral replication in patients with 2019 coronavirus disease (COVID-19). Here, we show that SARS-CoV-2 engages inflammasome and triggers pyroptosis in human monocytes, experimentally infected, and from patients under intensive care. Pyroptosis associated with caspase-1 activation, IL-1ß production, gasdermin D cleavage, and enhanced pro-inflammatory cytokine levels in human primary monocytes. At least in part, our results originally describe mechanisms by which monocytes, a central cellular component recruited from peripheral blood to respiratory tract, succumb to control severe COVID-19.

Reference

https://www.nature.com/articles/s41420-021-00428-w

Evaluation of myocardial injury patterns and ST changes among critical and non-critical patients with coronavirus-19 disease

Abstract

Novel coronavirus disease (COVID-19) has led to a major public health crisis globally. Currently, myocardial damage is speculated to be associated with COVID-19, which can be seen as one of the main causes of death of patients with COVID-19. It was therefore, aimed to investigate the effects of COVID-19 disease on myocardial injury in hospitalized patients who have been tested positive for COVID-19 pneumonia in this study. A prospective study was conducted among 201 patients with COVID-19 in the Pakistan Military Hospital from April 1 to August 31, 2020, including non-critical cases and critical cases. COVID-19 patients were stratified as critical and non-critical according to the signs and symptoms severity; with those requiring intensive care and invasive mechanical ventilation as critical, and those did not requiring invasive mechanical ventilation as non-critical. A total of 201 COVID-19 patients with critical and non-critical categories presented with myocardial injury. All patients with myocardial injury had an elevation in CKMB and Troponin-I levels. Of these patients, 43.7% presented with new electrocardiography (ECG) changes, and ST depression was typically observed in 36.3% patients. In addition, 18.7% patients presented with abnormal echocardiography findings, with right ventricular dilatation and dysfunction commonly seen among critical group patients. Results analyzed by a logistic regression model showing COVID-19 direct contribution to myocardial injury in these patients. COVID-19 disease directly leads to cardiovascular damage among critical and non-critical patients. Myocardial injury is associated not only with abnormal ECG changes but also with myocardial dysfunction on echocardiography and more commonly observed among critical patients.

Reference

https://www.nature.com/articles/s41598-021-84467-4

S-Trimer, a COVID-19 subunit vaccine candidate, induces protective immunity in nonhuman primates

Abstract

SARS-CoV-2 is the underlying cause for the COVID-19 pandemic. Like most enveloped RNA viruses, SARS-CoV-2 uses a homotrimeric surface antigen to gain entry into host cells. Here we describe S-Trimer, a native-like trimeric subunit vaccine candidate for COVID-19 based on Trimer-Tag technology. Immunization of S-Trimer with either AS03 (oil-in-water emulsion) or CpG 1018 (TLR9 agonist) plus alum adjuvants induced high-level of neutralizing antibodies and Th1-biased cellular immune responses in animal models. Moreover, rhesus macaques immunized with adjuvanted S-Trimer were protected from SARS-CoV-2 challenge compared to vehicle controls, based on clinical observations and reduction of viral loads in lungs. Trimer-Tag may be an important platform technology for scalable production and rapid development of safe and effective subunit vaccines against current and future emerging RNA viruses.

Reference

https://www.nature.com/articles/s41467-021-21634-1

Oncologic immunomodulatory agents in patients with cancer and COVID-19

Abstract

Corticosteroids, anti-CD20 agents, immunotherapies, and cytotoxic chemotherapy are commonly used in the treatment of patients with cancer. It is unclear how these agents affect patients with cancer who are infected with SARS-CoV-2. Retrospectively associations between SARS-CoV-2-associated respiratory failure or death were investigated, with receipt of the aforementioned medications and with pre-COVID-19 neutropenia. The study included all cancer patients diagnosed with SARS-CoV-2 at Memorial Sloan Kettering Cancer Center until June 2, 2020 (N = 820). We controlled for cancer-related characteristics known to predispose to worse COVID-19 as well as level of respiratory support during corticosteroid administration. Corticosteroid administration was associated with worse outcomes prior to use of supplemental oxygen; no statistically significant difference was observed in sicker cohorts. In patients with metastatic thoracic cancer, 9 of 25 (36%) and 10 of 31 (32%) had respiratory failure or

death among those who did and did not receive immunotherapy, respectively. Seven of 23 (30%) and 52 of 187 (28%) patients with hematologic cancer had respiratory failure or death among those who did and did not receive anti-CD20 therapy, respectively. Chemotherapy itself was not associated with worse outcomes, but pre-COVID-19 neutropenia was associated with worse COVID-19 course. Relative prevalence of chemotherapy-associated neutropenia in previous studies may account for different conclusions regarding the risks of chemotherapy in patients with COVID-19. In the absence of prospective studies and evidence-based guidelines, our data may aid providers looking to assess the risks and benefits of these agents in caring for cancer patients in the COVID-19 era.

Reference

https://www.nature.com/articles/s41598-021-84137-5

Ferritin is associated with the severity of lung involvement but not with worse prognosis in patients with COVID-19: Data from two Italian COVID-19 units

Abstract

The coronavirus 2019 disease (COVID-19) is characterised by a heterogeneous clinical presentation, a complex pathophysiology and a wide range of imaging findings, depending on disease severity and time course. A retrospective evaluation of hospitalized patients was conducted with proven SARS-CoV-2 infection, clinical signs of COVID-19 and computed tomography (CT) scan-proven pulmonary involvement, in order to identify relationships between clinical, serological, imaging data and disease outcomes in patients with COVID-19. Clinical and serological records of patients admitted to two COVID-19 Units of the Abruzzo region in Italy with proven SARS-CoV-2 pulmonary involvement investigated with CT scan, assessed at the time of admission to the hospital, were retrospectively evaluated. Sixty-one patients (22 females and 39 males) of median age 65 years were enrolled. Fifty-six patients were discharged while death occurred in 5 patients. None of the lung abnormalities detected by CT was different between discharged and deceased patients. No differences were observed in the features and extent of pulmonary involvement according to age and gender. Logistic regression analysis with age and gender as covariates demonstrated that ferritin levels over the 25th percentile were associated with the involvement of all 5 pulmonary lobes

(OR = 14.5, 95% CI 2.3–90.9, p = 0.004), the presence of septal thickening (OR = 8.2, 95% CI 1.6–40.9, p = 0.011) and the presence of mediastinal lymph node enlargement (OR = 12.0, 95% CI 1.1–127.5, p = 0.039) independently of age and gender. It was demonstrated that ferritin levels over the 25th percentile are associated with a more severe pulmonary involvement, independently of age and gender and not associated with disease outcomes. The identification of reliable biomarkers in patients with COVID-19 may help guiding clinical decision, tailoring therapeutic approaches and ultimately improving the care and prognosis of patients with this disease.

Reference

https://www.nature.com/articles/s41598-021-83831-8

Quality of life in the COVID-19 outbreak: Influence of psychological distress, government strategies, social distancing, and emotional recovery

Abstract

Considering the severity of the effects of COVID-19 on psychological health and quality of life, the present study investigates the direct effects of government strategies and social distancing and the moderating effect of emotional recovery on psychological distress and quality of life using the tenets of the theory of attachment and learned helplessness. The snowball sampling technique was used to recruit respondents from Bangladesh who completed a self-administered questionnaire via Google Forms, which provided cross-sectional data. The results revealed that both social distancing and government strategies have significant negative influences on psychological distress. Besides, government strategies have a significant positive influence on social distancing. Although psychological distress has a significant negative influence on quality of life, emotional recovery shows no moderating effect on the relationship between psychological distress and quality of life during the COVID-19 pandemic. The study provides insights for regulatory bodies and policymakers for developing effective policy interventions to ensure the well-being of people during this pandemic. Finally, the study highlights the implications for both theory and practice and a few notes for further research.

Reference

https://www.cell.com/heliyon/fulltext/S2405-8440(21)00512-0

Targeting androgen regulation of TMPRSS2 and ACE2 as a therapeutic strategy to combat COVID-19

Abstract

Epidemiological data showing increased severity and mortality of COVID-19 in men suggests a potential role for androgen in SARS-CoV-2 infection. Here, evidence for the transcriptional regulation of SARS-CoV-2 host cell receptor ACE2 and TMPRSS2 was presented, by androgen in mouse and human cells. Additionally, the endogenous interaction between TMPRSS2 and ACE2 in human cells was demonstrated and ACE2 as a TMPRSS2 substrate was validated. Further, Camostat – a TMPRSS2 inhibitor, blocked the cleavage of pseudotype SARS-CoV-2 surface Spike without disrupting TMPRSS2-ACE2 interaction. Thus providing evidence for the first time a direct role of TMPRSS2 in priming the SARS-CoV-2 Spike, required for viral fusion to the host cell. Importantly, androgen-deprivation, anti-androgens, or Camostat attenuated the SARS-CoV-2 S-mediated cellular entry. Together, our data provide a strong rationale for clinical evaluations of TMPRSS2 inhibitors, androgen-deprivation therapy/androgen receptor antagonists alone or in combination with antiviral drugs as early as clinically possible to prevent COVID-19 progression.

Reference

https://www.cell.com/iscience/fulltext/S2589-0042(21)00222-4

The study of antiviral drugs targeting SARS-CoV-2 nucleocapsid and spike proteins through large-scale compound repurposing

Abstract

Background: SARS-CoV-2 serology is used to identify prior infection at individual and at

Contributing to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) clinical treatment, a drug library encompassing approximately 3,142 clinical-stage or FDA-approved small molecules is profiled to identify the candidate therapeutic inhibitors targeting nucleocapsid protein (N) and spike protein (S) of SARS-CoV-2.

16 screened candidates with higher binding affinity are evaluated via virtual screening. Comparing to those under trial/temporarily used antivirus drugs (i.e., umifenovir, lopinavir), ceftriaxone, cefotaxime, and cefuroxime show higher binding affinities to the N-terminal domain of N protein (N-NTD), C-terminal domain of N protein (N-CTD), and receptor-binding domain of S protein (S-RBD). Cefotaxime and cefuroxime have high binding affinities towards S-RBD with angiotensin-converting enzyme 2 (ACE2) complex via influence the critical interface sites at the interface of S-RBD (Arg403, Tyr453, Trp495, Gly496, Phe497, Asn501and Tyr505) and ACE2 (Asn33, His34, Glu37, Asp38, Lys353, Ala386, Ala387, Gln388, Pro389, Phe390 and Arg393) complex.

Reference

https://www.cell.com/heliyon/fulltext/S2405-8440(21)00492-8

Time series analysis and mechanistic modelling of heterogeneity and sero-reversion in antibody responses to mild SARS-CoV-2 infection

Abstract

Background: SARS-CoV-2 serology is used to identify prior infection at individual and at population level. Extended longitudinal studies with multi-timepoint sampling to evaluate dynamic changes in antibody levels are required to identify the time horizon in which these applications of serology are valid, and to explore the longevity of protective humoral immunity.

Methods: Healthcare workers were recruited to a prospective cohort study from the first SARS-CoV-2 epidemic peak in London, undergoing weekly symptom screen, viral PCR and blood sampling over 16–21 weeks. Serological analysis (n =12,990) was performed using semi-quantitative Euroimmun IgG to viral spike S1 domain and Roche total antibody to viral nucleocapsid protein (NP) assays. Comparisons were made to pseudovirus neutralizing antibody measurements.

Findings: A total of 157/729 (21.5%) participants developed positive SARS-CoV-2 serology by one or other assay, of whom 31.0% were asymptomatic and there were no deaths. Peak Euroimmun anti-S1 and Roche anti-NP measurements correlated ($r = 0.57$, $p<0.0001$) but only anti-S1 measurements correlated with near-contemporary pseudovirus neutralising antibody titres (measured at 16–18 weeks, $r = 0.57$, $p<0.0001$).

By 21 weeks' follow-up, 31/143 (21.7%) anti-S1 and 6/150 (4.0%) anti-NP measurements reverted to negative. Mathematical modelling revealed faster clearance of anti-S1 compared to anti-NP (median half-life of 2.5 weeks versus 4.0 weeks), earlier transition to lower levels of antibody production (median of 8 versus 13 weeks), and greater reductions in relative antibody production rate after the transition (median of 35% versus 50%).

Interpretation: Mild SARS-CoV-2 infection is associated with heterogeneous serological responses in Euroimmun anti-S1 and Roche anti-NP assays. Anti-S1 responses showed faster rates of clearance, more rapid transition from high to low level production rate and greater reduction in production rate after this transition. In mild infection, anti-S1 serology alone may underestimate incident infections. The mechanisms that underpin faster clearance and lower rates of sustained anti-S1 production may impact on the longevity of humoral immunity.

Reference

https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(21)00052-9/fulltext

Epidemiology and clinical features of COVID-19 outbreaks in aged care facilities: A systematic review and meta-analysis

Abstract

Background: COVID-19 outbreaks in aged care facilities (ACFs) often have devastating consequences. However, epidemiologically these outbreaks are not well defined. We aimed to define such outbreaks in ACFs by systematically reviewing literature published during the current COVID-19 pandemic.

Methods: 11 Bibliographic databases were searched for literature published on COVID-19 in ACFs between December 2019 and September 2020. Original studies reporting extractable epidemiological data as part of outbreak investigations or non-outbreak surveillance of ACFs were included in this systematic review and meta-analysis. PROSPERO registration: CRD42020211424.

Findings: 5,148 Publications and selected 49 studies were identified from four continents reporting data on 214,380 residents in 8,502 ACFs with 25,567 confirmed cases of COVID-19. Aged care residents form a distinct vulnerable population with

single-facility attack rates of 45% [95% CI 32–58%] and case fatality rates of 23% [95% CI 18–28%]. Of the cases, 31% [95% CI 28–34%] were asymptomatic. The rate of hospitalization amongst residents was 37% [95% CI 35–39%]. Data from 21 outbreaks identified a resident as the index case in 58% of outbreaks and a staff member in 42%. Findings from the included studies were heterogeneous and of low to moderate quality in risk of bias assessment.

Interpretation: The clinical presentation of COVID-19 varies widely in ACFs residents, from asymptomatic to highly serious cases. Preventing the introduction of COVID-19 into ACFs is key, and both residents and staff are a priority group for COVID-19 vaccination. Rapid diagnosis, identification of primary and secondary cases and close contacts plus their isolation and quarantine are of paramount importance.

Reference

https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00051-1/fulltext

Publication Date: Feb 27, 2021

In silico **analysis of altered expression of long non-coding RNA in SARS-CoV-2 infected cells and their possible regulation by STAT1, STAT3 and interferon regulatory factors**

Abstract

Altered expression of long noncoding RNA (lncRNA), longer than 200 nucleotides without potential for coding protein, has been observed in diverse human diseases including viral diseases. It is largely unknown whether lncRNA would deregulate in SARS-CoV-2 infection, causing ongoing pandemic COVID-19. To identify, if lncRNA was deregulated in SARS-CoV-2 infected cells, *in silico* the data in GSE147507 were analyzed. It was revealed that expression of 20 lncRNA like MALAT1, NEAT1 was increased and 4 lncRNA like PART1, TP53TG1 was decreased in at least two independent cell lines infected with SARS-CoV-2. Expression of NEAT1 was also increased in lungs tissue of COVID-19 patients. The deregulated lncRNA could interact with more than 2800 genes/proteins and 422 microRNAs as revealed from the database that catalogs experimentally determined interactions. Analysis with the interacting gene/protein partners of deregulated lncRNAs revealed that these genes/proteins were

associated with many pathways related to viral infection, inflammation and immune functions. To find out whether these lncRNAs could be regulated by STATs and interferon regulatory factors (IRFs), ChIPBase v2.0 was used that catalogs experimentally determined binding from ChIP-seq data. It was revealed that any one of the transcription factors IRF1, IRF4, STAT1, STAT3 and STAT5A had experimentally determined binding at regions within -5kb to +1kb of the deregulated lncRNAs in at least 2 independent cell lines/conditions. Our analysis revealed that several lncRNAs could be regulated by IRF1, IRF4 STAT1 and STAT3 in response to SARS-CoV-2 infection and lncRNAs might be involved in antiviral response. However, these in silico observations are necessary to be validated experimentally.

Reference

https://www.cell.com/heliyon/fulltext/S2405-8440(21)00500-4

SARS-CoV-2 transmission risk from asymptomatic carriers: Results from a mass screening programme in Luxembourg

Abstract

Background: To accompany the lifting of COVID-19 lockdown measures, Luxembourg implemented a mass screening (MS) programme. The first phase coincided with an early summer epidemic wave in 2020.

Methods: rRT-PCR-based screening for SARS-CoV-2 was performed by pooling of samples. The infrastructure allowed the testing of the entire resident and cross-border worker populations. The strategy relied on social connectivity within different activity sectors. Invitation frequencies were tactically increased in sectors and regions with higher prevalence. The results were analysed alongside contact tracing data.

Findings: The voluntary programme covered 49% of the resident and 22% of the cross-border worker populations. It identified 850 index cases with an additional 249 cases from contact tracing. Over-representation was observed in the services, hospitality and construction sectors alongside regional differences. Asymptomatic cases had a significant but lower secondary attack rate when compared to symptomatic individuals. Based on simulations using an agent-based SEIR model, the total number of expected

cases would have been 42·9% (90% CI [-0·3, 96·7]) higher without MS. Mandatory participation would have resulted in a further difference of 39·7% [19·6, 59·2].

Interpretation: Strategic and tactical MS allows the suppression of epidemic dynamics. Asymptomatic carriers represent a significant risk for transmission. Containment of future outbreaks will depend on early testing in sectors and regions. Higher participation rates must be assured through targeted incentivisation and recurrent invitation.

Reference

https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762(21)00033-8/fulltext

Publication Date: Feb 26, 2021

Metabolic programs define dysfunctional immune responses in severe COVID-19 patients

Abstract

It is unclear why some SARS-CoV-2 patients readily resolve infection while others develop severe disease. By interrogating metabolic programs of immune cells in severe and recovered coronavirus disease 2019 (COVID-19) patients compared with other viral infections, we identify a unique population of T cells. These T cells express increased Voltage-Dependent Anion Channel 1 (VDAC1), accompanied by gene programs and functional characteristics linked to mitochondrial dysfunction and apoptosis. The percentage of these cells increases in elderly patients and correlates with lymphopenia. Importantly, T cell apoptosis is inhibited in vitro by targeting the oligomerization of VDAC1 or blocking caspase activity. an expansion of myeloid-derived suppressor cells was also observed with unique metabolic phenotypes specific to COVID-19, and their presence distinguishes severe from mild disease. Overall, the identification of these metabolic phenotypes provides insight into the dysfunctional immune response in acutely ill COVID-19 patients and provides a means to predict and track disease severity and/or design metabolic therapeutic regimens.

Reference

https://www.cell.com/cell-reports/fulltext/S2211-1247(21)00177-7

Shorter androgen receptor polyQ alleles protect against life-threatening COVID-19 disease in European males

Abstract

Background: While SARS-CoV-2 similarly infects men and women, COVID-19 outcome is less favorable in men. Variability in COVID-19 severity may be explained by differences in the host genome.

Methods: Poly-amino acids variability were compared from WES data in severely affected COVID-19 patients versus SARS-CoV-2 PCR-positive oligo-asymptomatic subjects.

Findings: Shorter polyQ alleles (≤22) in the androgen receptor (AR) conferred protection against severe outcome in COVID-19 in the first tested cohort (both males and females) of 638 Italian subjects. The association between long polyQ alleles (≥23) and severe clinical outcome ($p = 0.024$) was also validated in an independent cohort of Spanish men <60 years of age ($p = 0.014$). Testosterone was higher in subjects with AR long-polyQ, possibly indicating receptor resistance ($p = 0.042$ Mann-Whitney U test). Inappropriately low serum testosterone level among carriers of the long-polyQ alleles ($p = 0.0004$ Mann-Whitney U test) predicted the need for intensive care in COVID-19 infected men. In agreement with the known anti-inflammatory action of testosterone, patients with long-polyQ and age ≥60 years had increased levels of CRP ($p = 0.018$, not accounting for multiple testing).

Interpretation: The first genetic polymorphism were identified that appears to predispose some men to develop more severe disease. Failure of the endocrine feedback to overcome AR signaling defects by increasing testosterone levels during the infection leads to the polyQ tract becoming dominant to serum testosterone levels for the clinical outcome. These results may contribute to designing reliable clinical and public health measures and provide a rationale to test testosterone as adjuvant therapy in men with COVID-19 expressing long AR polyQ repeats.

Reference

https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(21)00039-6/fulltext

Hydroxychloroquine with or without azithromycin for treatment of early SARS-CoV-2 infection among high-risk outpatient adults: A randomized clinical trial

Abstract

Background: Treatment options for outpatients with COVID-19 could reduce morbidity and prevent SARS-CoV-2 transmission.

Methods: In this randomized, double-blind, three-arm (1:1:1) placebo-equivalent controlled trial conducted remotely throughout the United States, adult outpatients with laboratory-confirmed SARS-CoV-2 infection were recruited. Participants were randomly assigned to receive hydroxychloroquine (HCQ) (400 mg BID x1day, followed by 200 mg BID x9days) with or without azithromycin (AZ) (500 mg, then 250 mg daily x4days) or placebo-equivalent (ascorbic acid (HCQ) and folic acid (AZ)), stratified by risk for progression to severe COVID-19 (high-risk vs. low-risk). Self-collected nasal swabs for SARS-CoV-2 PCR, FLUPro symptom surveys, EKGs and vital signs were collected daily. Primary endpoints were: (a) 14-day progression to lower respiratory tract infection (LRTI), 28-day COVID-19 related hospitalization, or death; (b) 14-day time to viral clearance; secondary endpoints included time to symptom resolution (ClinicalTrials.gov: NCT04354428). Due to the low rate of clinical outcomes, the study was terminated for operational futility.

Findings: Between 15th April and 27th July 2020, 231 participants were enrolled and 219 initiated medication a median of 5.9 days after symptom onset. Among 129 high-risk participants, incident LRTI occurred in six (4.7%) participants (two control, four HCQ/AZ) and COVID-19 related hospitalization in seven (5.4%) (four control, one HCQ, two HCQ/AZ); no LRTI and two (2%) hospitalizations occurred in the 102 low-risk participants (one HCQ, one HCQ/AZ). There were no deaths. Among 152 participants with viral shedding at enrollment, median time to clearance was 5 days (95% CI=4–6) in HCQ, 6 days (95% CI=4–8) in HCQ/AZ, and 8 days (95% CI=6–10) in control. Viral clearance was faster in HCQ (HR=1.62, 95% CI=1.01–2.60, p = 0.047) but not HCQ/AZ (HR=1.25, p = 0.39) compared to control. Among 197 participants who met the COVID-19 definition at enrollment, time to symptom resolution did not differ by group (HCQ: HR=1.02, 95% CI-0.63–1.64, p = 0.95, HCQ/AZ: HR=0.91, 95% CI=0.57–1.45, p = 0.70).

Interpretation: Neither HCQ nor HCQ/AZ shortened the clinical course of outpatients with COVID-19, and HCQ, but not HCQ/AZ, had only a modest effect on SARS-CoV-2 viral shedding. HCQ and HCQ/AZ are not effective therapies for outpatient treatment of SARV-CoV-2 infection.

Reference

https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00053-5/fulltext

Publication Date: Feb 25, 2021

Structural insights into SARS-CoV-2 spike protein and its natural mutants found in Mexican population

Abstract

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a newly emerged coronavirus responsible for coronavirus disease 2019 (COVID-19); it become a pandemic since March 2020. To date, there have been described three lineages of SARS-CoV-2 circulating worldwide, two of them are found among Mexican population, within these, we observed three mutations of spike (S) protein located at amino acids H49Y, D614G, and T573I. To understand if these mutations could affect the structural behavior of S protein of SARS-CoV-2, as well as the binding with S protein inhibitors (cepharanthine, nelfinavir, and hydroxychloroquine), molecular dynamic simulations and molecular docking were employed. It was found that these punctual mutations affect considerably the structural behavior of the S protein compared to wild type, which also affect the binding of its inhibitors into their respective binding site. Thus, further experimental studies are needed to explore if these affectations have an impact on drug-S protein binding and its possible clinical effect.

Reference

https://www.nature.com/articles/s41598-021-84053-8

A syndromic surveillance tool to detect anomalous clusters of COVID-19 symptoms in the United States

Abstract

Coronavirus SARS-COV-2 infections continue to spread across the world, yet effective large-scale disease detection and prediction remain limited. COVID Control: A Johns Hopkins University Study, is a novel syndromic surveillance approach, which collects body temperature and COVID-like illness (CLI) symptoms across the US using a smartphone app and applies spatio-temporal clustering techniques and cross-correlation analysis to create maps of abnormal symptomatology incidence that are made publicly available. The results of the cross-correlation analysis identify optimal temporal lags between symptoms and a range of COVID-19 outcomes, with new taste/smell loss showing the highest correlations. We also identified temporal clusters of change in taste/smell entries and confirmed COVID-19 incidence in Baltimore City and County. Further, we utilized an extended simulated dataset to showcase our analytics in Maryland. The resulting clusters can serve as indicators of emerging COVID-19 outbreaks, and support syndromic surveillance as an early warning system for disease prevention and control.

Reference

https://www.nature.com/articles/s41598-021-84145-5

Estimating risk of mechanical ventilation and in-hospital mortality among adult COVID-19 patients admitted to Mass General Brigham: The VICE and DICE scores

Abstract

Background: Risk stratification of COVID-19 patients upon hospital admission is key for their successful treatment and efficient utilization of hospital resources. The risk factors were evaluated on admission (including comorbidities, vital signs, and initial laboratory assessment) associated with ventilation need and in-hospital mortality in COVID-19.

Methods: a retrospective cohort of COVID-19 patients was established from Mass General Brigham hospitals. Demographic, clinical, and admission laboratory data were obtained from electronic medical records of patients admitted to the hospital with laboratory-confirmed COVID-19 before May 19, 2020. Multivariable logistic regression

analyses were used to construct and validate the Ventilation in COVID Estimator (VICE) and Death in COVID Estimator (DICE) risk scores.

Findings: The entire cohort included 1042 patients (median age, 64 years; 56.8% male). The derivation and validation cohorts for the risk scores included 578 and 464 patients, respectively. Four factors were found to be independently predictive for mechanical ventilation requirement (diabetes mellitus, SpO2:FiO2 ratio, C-reactive protein, and lactate dehydrogenase), and 10 factors to be predictors of in-hospital mortality (age, male sex, coronary artery disease, diabetes mellitus, chronic statin use, SpO_2:FiO_2 ratio, body mass index, neutrophil to lymphocyte ratio, platelet count, and procalcitonin). Using these factors, the VICE and DICE risk scores were constructed, which performed with C-statistics of 0.84 and 0.91, respectively. Importantly, the chronic use of a statin was associated with protection against death due to COVID-19. The VICE and DICE score calculators have been placed on an interactive website freely available to healthcare providers and researchers (https://covid-calculator.com/).

Interpretation: The risk scores developed in this study may help clinicians more appropriately determine which COVID-19 patients will need to be managed with greater intensity.

Reference

https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00045-6/fulltext

A Neanderthal OAS1 isoform protects individuals of European ancestry against COVID-19 susceptibility and severity

Abstract

To identify circulating proteins influencing Coronavirus Disease 2019 (COVID-19) susceptibility and severity, we undertook a two-sample Mendelian randomization (MR) study, rapidly scanning hundreds of circulating proteins while reducing bias due to reverse causation and confounding. In up to 14,134 cases and 1.2 million controls, we found that an S.D. increase in OAS1 levels was associated with reduced COVID-19 death or ventilation (odds ratio (OR) = 0.54, $P = 7 \times 10^{-8}$), hospitalization (OR = 0.61, $P = 8 \times 10^{-8}$) and susceptibility (OR = 0.78, $P = 8 \times 10^{-6}$). Measuring OAS1 levels in 504 individuals, higher plasma OAS1 levels were found in a non-infectious

state were associated with reduced COVID-19 susceptibility and severity. Further analyses suggested that a Neanderthal isoform of OAS1 in individuals of European ancestry affords this protection. Thus, evidence from MR and a case–control study support a protective role for OAS1 in COVID-19 adverse outcomes. Available pharmacological agents that increase OAS1 levels could be prioritized for drug development.

Reference

https://www.nature.com/articles/s41591-021-01281-1

Infection and transmission of SARS-CoV-2 in London care homes reporting no cases or outbreaks of COVID-19: Prospective observational cohort study, England 2020

Abstract

Background: Care homes have been disproportionately affected by the COVID-19 pandemic. The potential role of asymptomatic infection and silent transmission were investigated in London care homes that reported no cases of COVID-19 during the first wave of the pandemic.

Methods: Five care homes with no cases and two care homes reporting a single case of COVID-19 (non-outbreak homes) were investigated with nasal swabbing for SARS-CoV-2 RT-PCR and serology for SARS-CoV-2 antibodies five weeks later. Whole genome sequencing (WGS) was performed on RT-PCR positive samples. Serology results were compared with those of six care homes with recognised outbreaks.

Findings: Across seven non-outbreak homes, 718 (387 staff, 331 residents) individuals had a nasal swab and 651 (386 staff, 265 residents) had follow-up serology. Sixteen individuals (13 residents, 3 staff) in five care homes with no reported cases were RT-PCR positive (care home positivity rates, 0 to 7.6%) compared to 13 individuals (3.0 and 10.8% positivity) in two homes reporting a single case. Seropositivity across these seven homes varied between 10.7-56.5%, with four exceeding community seroprevalence in London (14.8%). Seropositivity rates for staff and residents correlated significantly (rs 0.84, [95% CI 0.51-0.95] p <0.001) across the 13 homes. WGS

identified multiple introductions into some homes and silent transmission of a single lineage between staff and residents in one home.

Interpretation: High rates of asymptomatic infection and transmission were found, even in care homes with no COVID-19 cases. The higher seropositivity rates compared to RT-PCR positivity highlights the true extent of the silent outbreak.

Reference

https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762(21)00015-6/fulltext

PERSPECTIVE

Publication Date: Feb 26, 2021

SARS-CoV-2 dependence on host pathways

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) first emerged in 2019, and its high pathogenicity, infectivity, and transmissibility have led to a global pandemic. Although several vaccines have been approved in different countries, most of the global population currently remains unvaccinated because of disparities in vaccine distribution and limited manufacturing capabilities. Owing to a lack of treatment options (particularly in low- and middle-income countries), the slow progression of vaccination, and the emergence of SARS-CoV-2 variants that elicit reduced responses to vaccines, there is an urgent need to identify therapeutics to reduce COVID-19 morbidity and mortality. White et al. demonstrate that the small-molecule drug, plitidepsin, which is approved to treat relapsed and refractory multiple myeloma, possesses antiviral activity against SARS-CoV-2 and may be a promising drug candidate for treating COVID-19. This suggests that antivirals discovered in the race to treat COVID-19 may be useful for future epidemics. For more details, read the link given below.

Reference

https://science.sciencemag.org/content/371/6532/884

COMMENT

Publication Date: Mar 03, 2021

Preparing for COVID-19 vaccine roll-out through simulation exercises

Abstract

As the COVID-19 pandemic reached over 97 million cases and exceeded 2 million deaths globally only 1 year after its emergence several candidate vaccines have shown promising efficacy and safety profiles, with some already approved for emergency use and rolled out globally. At this juncture, it is critical that the national deployment and vaccination plans are carefully crafted as recommended in the WHO guidance on developing a national deployment and vaccination plans for COVID-19 vaccines. Countries need to be ready to carry out unprecedented mass vaccination, including having procedures in place for national regulatory agencies to approve vaccines for emergency use; coordination systems between national regulatory agencies and import control entities; communication strategies to address rumours and misinformation to combat vaccine hesitancy; systems for the monitoring and management of adverse events following immunisation; and logistics and delivery systems for maintaining cold chains. For more details, read the link given below.

Reference

https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(21)00051-6/fulltext

Publication Date: Mar 01, 2021

Understanding the survivorship burden of long COVID

Emerging evidence suggests that upwards of 20% of all SARS-CoV-2 positive individuals continue to experience chronic and debilitating symptoms, known either as ‘long COVID’ or ‘post COVID syndrome’, following the resolution of their initial infection. Despite this sizeable cohort, there have been limited coordinated attempts to understand the overall survivorship burden associated with this condition.

The concept of ‘survivorship’ provides healthcare professionals, researchers and policy makers with a communal lens through which they may frame holistic interventions

aimed at reducing the overall burden of living through a condition. This term encompasses the physiological, psychological, social, functional and economic impact of living with a chronic condition for an affected individual and their family members/caregivers. Despite its predominant use in oncological literature, we can draw several parallels between the journey of long COVID and many cancers; both patient cohorts typically describe (i) the psychological impact of an unexpected diagnosis and duration of symptoms; (ii) a complex set of evolving physical symptoms; (iii) on-going changes in physical function; and (iv) an associated change in lifestyle, finances and interpersonal relationships. For more details, read the link given below.

Reference

https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00047-X/fulltext

CORRESPONDANCE

Publication Date: Mar 02, 2021

COVID-19 intra-action reviews: Potential for a sustained response plan

Landry Ndriko Mayigane and colleagues' call (December, 2020) for countries to plan and conduct intra-action reviews regularly throughout the COVID-19 response. An intra-action review is a country-led process that reviews past response actions to identify crucial gaps and optimise response plans going forward. WHO guidance for conducting a country COVID-19 intra-action review includes more than 300 discussion questions that can be adapted to a country's context.

However, given that 26 of 33 countries that have already completed an intra-action review are experiencing ongoing SARS-CoV-2 transmission at the time of writing, the retrospective intra-action review process does not sufficiently address ongoing and protracted response planning. Within this context, the inclusion of a prospective response examination was advocated in the intra-action review process—*i.e.*, examining how to sustain response measures to ensure resiliency and plan effectively for the future. For more details, read the link given below.

Reference

https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(21)00078-4/fulltext

An interactive website tracking COVID-19 vaccine development

The urgent need for effective vaccines has prompted vaccine developers to pivot towards COVID-19, resulting in rapid growth of preclinical candidates (appendix) and an accelerated vaccine development pipeline. In response to the unfolding pandemic and the extraordinary volume and pace of global vaccine research, an online, interactive vaccine tracker was developed hosted by the Vaccine Centre (VaC) at the London School of Hygiene and Tropical Medicine (LSHTM; London, UK). Launched in April 2020, this tracker aims to collate up-to-date information on all COVID-19 vaccine candidates from inception through to deployment, enabling policy makers, researchers, and the public to keep informed of the rapid developments. All code and underlying data

for the tracker are freely available and are updated regularly through a Github repository. For more details, read the link given below.

Reference

https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(21)00043-7/fulltext

Antibody response to first BNT162b2 dose in previously SARS-CoV-2-infected individuals

Rapid vaccine-induced population immunity is a key global strategy to control COVID-19. Vaccination programmes must maximise early impact, particularly with accelerated spread of new variants. Most vaccine platforms use a two-dose prime-boost approach to generate an immune response against the virus S1 spike protein, the titres of which correlate with functional virus neutralisation and increase with boosting. To enable larger numbers of people to receive the first dose, delayed administration of the second dose has been advocated and implemented by some. The impact of previous SARS-CoV-2 infection on the need for boosting is not known.

It was reasoned that previous infection could be analogous to immune priming. As such, a first prime vaccine dose would effectively act as boost, so a second dose might not be needed. To test this, a nested case-control analysis of 51 participants of COVIDsortium was undertooked, an ongoing longitudinal observational study of health-care workers (HCWs) in London who underwent weekly PCR and quantitative serology testing from the day of the first UK lockdown on March 23, 2020, and for 16 weeks onwards. 24 of 51 HCWs had a previous laboratory-confirmed mild or asymptomatic SARS-CoV-2 infection, as confirmed by positive detection of antibodies against the SARS-CoV-2 nucleocapsid (Elecsys Anti-SARS-CoV-2 N ECLIA, Roche Diagnostics, Burgess Hill, UK) or the receptor binding domain of the SARS-CoV-2 S1 subunit of the spike protein (anti-S; Elecsys anti-SARS-CoV-2 spike ECLIA, Roche Diagnostics), whereas 27 HCWs remained seronegative. A median of 12·5 sampling timepoints per participant permitted the identification of peak antibody titres in seropositive individuals while avoiding false negatives. For more details, read the link given below.

Reference

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00501-8/fulltext

Effect of previous SARS-CoV-2 infection on humoral and T-cell responses to single-dose BNT162b2 vaccine

The rapid implementation of SARS-CoV-2 vaccination is now a global health-care priority. Successful phase 3 trial outcomes have been reported for numerous vaccines that induce robust humoral and cellular immune responses against the SARS-CoV-2 spike protein. To gain rapid control of accelerating cases and maximise public health impact, the UK Government has adopted the strategy of delaying second vaccination to 12 weeks. This policy has generated controversy, particularly among health-care workers (HCWs), the majority of whom have received BNT162b2 mRNA vaccine.

Limited data on immune responses to single-dose vaccination with BNT162b2 are available, and vaccine responses following previous natural infection have not been assessed in clinical trials. Therefore immunological responses to single-dose BNT162b2 were investigated using a combination of serology, live virus neutralisation, and T-cell enzyme-linked immunospot (ELISpot) assays. For more details, read the link given below.

Reference

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00502-X/fulltext

REPORT

Publication Date: Feb 25, 2021

Low awareness of past SARS-CoV-2 infection in healthy plasma donors

Awareness of infection with SARS-CoV-2 is crucial for the effectiveness of COVID-19 control measures. Here, we investigate awareness of infection and symptoms in relation to antibodies against SARS-CoV-2 in healthy plasma donors. We asked individuals donating plasma across the Netherlands between May 11th and 18th 2020 to report COVID-19-related symptoms, and we tested for antibodies indicative of a past infection with SARS-CoV-2. Among 3,676 with antibodies, and from questionnaire data, 239 (6.5%) are positive for SARS-CoV-2 antibodies. Of those, 48% suspect no COVID-19, despite the majority reporting symptoms; 11% of seropositive individuals report no symptoms and 27% very mild symptoms at any time during the first peak of the epidemic. Anosmia/ageusia and fever are most strongly associated with seropositivity. Almost half of seropositive individuals do not suspect SARS-CoV-2 infection. Improved recognition of COVID-19 symptoms, in particular, anosmia/ageusia and fever, is needed to reduce widespread SARS-CoV-2 transmission.

Reference

https://www.cell.com/cell-reports-medicine/fulltext/S2666-3791(21)00038-0