RESEARCH PUBLICATIONS

Advancements in detection of SARS-CoV-2 infection for confronting COVID-19 pandemics

Abstract

As one of the major approaches in combating the COVID-19 pandemics, the availability of specific and reliable assays for the SARS-CoV-2 viral genome and its proteins is essential to identify the infection in suspected populations, make diagnoses in symptomatic or asymptomatic individuals, and determine clearance of the virus after the infection. For these purposes, use of the quantitative reverse transcriptase polymerase chain reaction (qRT-PCR) for detection of the viral nucleic acid remains the most valuable in terms of its specificity, fast turn-around, high-throughput capacity, and reliability. It is critical to update the sequences of primers and probes to ensure the detection of newly emerged variants. Various assays for increased levels of IgG or IgM antibodies are available for detecting ongoing or past infection, vaccination responses, and persistence and for identifying high titers of neutralizing antibodies in recovered individuals. Viral genome sequencing is increasingly used for tracing infectious sources, monitoring mutations, and subtype classification and is less valuable in diagnosis because of its capacity and high cost. Nanopore target sequencing with portable options is available for a quick process for sequencing data. Emerging CRISPR-Cas-based assays, such as SHERLOCK and AIOD-CRISPR, for viral genome detection may offer options for prompt and point-of-care detection. Moreover, aptamer-based probes may be multifaceted for developing portable and high-throughput assays with fluorescent or chemiluminescent probes for viral proteins. In conclusion, assays are available for viral genome and protein detection, and the selection of specific assays depends on the

purposes of prevention, diagnosis and pandemic control, or monitoring of vaccination efficacy.

Reference

https://www.nature.com/articles/s41374-021-00663-w

Interactions of anti-COVID-19 drug candidates with hepatic transporters may cause liver toxicity and affect pharmacokinetics

Abstract

Transporters in the human liver play a major role in the clearance of endo- and xenobiotics. Apical (canalicular) transporters extrude compounds to the bile, while basolateral hepatocyte transporters promote the uptake of, or expel, various compounds from/into the venous blood stream. In the present work, the *in vitro* interactions of some key repurposed drugs advocated to treat COVID-19 (lopinavir, ritonavir, ivermectin, remdesivir and favipiravir), with the key drug transporters of hepatocytes, were examined. These transporters included ABCB11/BSEP, ABCC2/MRP2, and SLC47A1/MATE1 in the canalicular membrane, as well as ABCC3/MRP3, ABCC4/MRP4, SLC22A1/OCT1, SLCO1B1/OATP1B1, SLCO1B3/OATP1B3, and SLC10A1/NTCP, residing in the basolateral membrane. Lopinavir and ritonavir in low micromolar concentrations inhibited BSEP and MATE1 exporters, as well as OATP1B1/1B3 uptake transporters. Ritonavir had a similar inhibitory pattern, also inhibiting OCT1. Remdesivir strongly inhibited MRP4, OATP1B1/1B3, MATE1 and OCT1. Favipiravir had no significant effect on any of these transporters. Since both general drug metabolism and drug-induced liver toxicity are strongly dependent on the functioning of these transporters, the various interactions reported here may have important clinical relevance in the drug treatment of this viral disease and the existing co-morbidities.

Reference

https://www.nature.com/articles/s41598-021-97160-3

Neutralizing antibodies for the prevention and treatment of COVID-19

Abstract

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) initiates the infection process by binding to the viral cellular receptor angiotensin-converting enzyme 2 through the receptor-binding domain (RBD) in the S1 subunit of the viral spike (S) protein. This event is followed by virus–cell membrane fusion mediated by the S2 subunit, which allows virus entry into the host cell. Therefore, the SARS-CoV-2 S protein is a key therapeutic target, and prevention and treatment of coronavirus disease 2019 (COVID-19) have focused on the development of neutralizing monoclonal antibodies (nAbs) that target this protein. In this review, the nAbs targeting SARS-CoV-2 proteins were summarized that have been developed to date, with a focus on the N-terminal domain and RBD of the S protein. The roles were also described that binding affinity, neutralizing activity, and protection provided by these nAbs play in the prevention and treatment of COVID-19 and discuss the potential to improve nAb efficiency against multiple SARS-CoV-2 variants. This review provides important information for the development of effective nAbs with broad-spectrum activity against current and future SARS-CoV-2 strains.

Reference

https://www.nature.com/articles/s41423-021-00752-2

Telaprevir is a potential drug for repurposing against SARS-CoV-2: Computational and *in vitro* studies

Abstract

Drug repurposing is an important approach to the assignment of already approved drugs for new indications. This technique bypasses some steps in the traditional drug approval system, which saves time and lives in the case of pandemics. Direct acting antivirals (DAAs) have repeatedly repurposed from treating one virus to another. In this study, 16 FDA-approved hepatitis C virus (HCV) DAA drugs were studied to explore their activities against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) human and viral targets. Among the 16 HCV DAA drugs, telaprevir has shown the best *in silico* evidence to work on both indirect human targets (cathepsin L [CTSL] and

human angiotensin-converting enzyme 2 [hACE2] receptor) and direct viral targets (main protease [Mpro]). Moreover, the docked poses of telaprevir inside both hACE2 and Mpro were subjected to additional molecular dynamics simulations monitored by calculating the binding free energy using MM-GBSA. In vitro analysis of telaprevir showed inhibition of SARS-CoV-2 replication in cell culture (IC_{50} = 11.552 μM, CC_{50} = 60.865 μM, and selectivity index = 5.27). Accordingly, based on the *in silico* studies and supported by the presented in vitro analysis, we suggest that telaprevir may be considered for therapeutic development against SARS-CoV-2.

Reference

https://www.cell.com/heliyon/fulltext/S2405-8440(21)02065-X

Genomics, social media and mobile phone data enable mapping of SARS-CoV-2 lineages to inform health policy in Bangladesh

Abstract

Genomics, combined with population mobility data, used to map importation and spatial spread of SARS-CoV-2 in high-income countries has enabled the implementation of local control measures. Here, to track the spread of SARS-CoV-2 lineages in Bangladesh at the national level, outbreak trajectory and variant emergence using genomics, Facebook 'Data for Good' and data from three mobile phone operators, were analysed. The complete genomes of 67 SARS-CoV-2 samples (collected by the IEDCR in Bangladesh between March and July 2020) were sequenced and combined these data with 324 publicly available Global Initiative on Sharing All Influenza Data (GISAID) SARS-CoV-2 genomes from Bangladesh at that time. It was found that most (85%) of the sequenced isolates were Pango lineage B.1.1.25 (58%), B.1.1 (19%) or B.1.36 (8%) in early-mid 2020. Bayesian time-scaled phylogenetic analysis predicted that SARS-CoV-2 first emerged during mid-February in Bangladesh, from abroad, with the first case of coronavirus disease 2019 (COVID-19) reported on 8 March 2020. At the end of March 2020, three discrete lineages expanded and spread clonally across Bangladesh. The shifting pattern of viral diversity in Bangladesh, combined with the mobility data, revealed that the mass migration of people from cities to rural areas at the end of March, followed by frequent travel between Dhaka (the capital of Bangladesh) and the rest of the country, disseminated three dominant viral lineages. Further analysis of an

additional 85 genomes (November 2020 to April 2021) found that importation of variant of concern Beta (B.1.351) had occurred and that Beta had become dominant in Dhaka. Our interpretation that population mobility out of Dhaka, and travel from urban hotspots to rural areas, disseminated lineages in Bangladesh in the first wave continues to inform government policies to control national case numbers by limiting within-country travel.

Reference

https://www.nature.com/articles/s41564-021-00955-3

Conventional oxygen therapy versus CPAP as a ceiling of care in ward-based patients with COVID-19: A multi-centre cohort evaluation

Abstract

Background: Continuous positive airway pressure (CPAP) therapy is commonly used for respiratory failure due to severe COVID-19 pneumonitis, including in patients deemed not likely to benefit from invasive mechanical ventilation (nIMV). Little evidence exists demonstrating superiority over conventional oxygen therapy, whilst ward-level delivery of CPAP presents practical challenges. It was sought to compare clinical outcomes of oxygen therapy versus CPAP therapy in patients with COVID-19 who were nIMV.

Methods: This retrospective multi-centre cohort evaluation included patients diagnosed with COVID-19 who were nIMV, had a treatment escalation plan of ward-level care and clinical frailty scale ≤ 6. Recruitment occurred during the first two waves of the UK COVID-19 pandemic in 2020; from 1st March to May 31st, and from 1st September to 31st December. Patients given CPAP were compared to patients receiving oxygen therapy that required FiO_2 ≥0.4 for more than 12 hours at hospitals not providing ward-level CPAP. Logistic regression modelling was performed to compare 30-day mortality between treatment groups, accounting for important confounders and within-hospital clustering.

Findings: Seven hospitals provided data for 479 patients during the UK COVID-19 pandemic in 2020. Overall 30-day mortality was 75.6% in the oxygen group (186/246 patients) and 77.7% in the CPAP group (181/233 patients). A lack of evidence for a treatment effect persisted in the adjusted model (adjusted odds ratio 0.84 95% CI 0.57-

1.23, p=0.37). 49.8% of patients receiving CPAP-therapy (118/237) chose to discontinue it.

Interpretation: No survival difference was found between using oxygen alone or CPAP to treat patients with severe COVID-19 who were nIMV. A high patient-initiated discontinuation rate for CPAP suggests a significant treatment burden. Further reflection is warranted on the current treatment guidance and widespread application of CPAP in this setting.

Reference

https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00402-8/fulltext

A universal bacteriophage T4 nanoparticle platform to design multiplex SARS-CoV-2 vaccine candidates by CRISPR engineering

Abstract

A "universal" platform that can rapidly generate multiplex vaccine candidates is critically needed to control pandemics. Using the severe acute respiratory syndrome coronavirus 2 as a model, we have developed such a platform by CRISPR engineering of bacteriophage T4. A pipeline of vaccine candidates was engineered by incorporating various viral components into appropriate compartments of phage nanoparticle structure. These include expressible spike genes in genome, spike and envelope epitopes as surface decorations, and nucleocapsid proteins in packaged core. Phage decorated with spike trimers was found to be the most potent vaccine candidate in animal models. Without any adjuvant, this vaccine stimulated robust immune responses, both T helper cell 1 (TH1) and TH2 immunoglobulin G subclasses, blocked virus-receptor interactions, neutralized viral infection, and conferred complete protection against viral challenge. This new nanovaccine design framework might allow the rapid deployment of effective adjuvant-free phage-based vaccines against any emerging pathogen in the future.

Reference

https://www.science.org/doi/10.1126/sciadv.abh1547

Platelets amplify endotheliopathy in COVID-19

Abstract

Given the evidence for a hyperactive platelet phenotype in COVID-19, effector cell properties of COVID-19 platelets on endothelial cells (ECs) were investigated. Integration of EC and platelet RNA sequencing revealed that platelet-released factors in COVID-19 promote an inflammatory hypercoagulable endotheliopathy. We identified S100A8 and S100A9 as transcripts enriched in COVID-19 platelets and were induced by megakaryocyte infection with SARS-CoV-2. Consistent with increased gene expression, the heterodimer protein product of S100A8/A9, myeloid-related protein (MRP) 8/14, was released to a greater extent by platelets from COVID-19 patients relative to controls. It was demonstrated that platelet-derived MRP8/14 activates ECs, promotes an inflammatory hypercoagulable phenotype, and is a significant contributor to poor clinical outcomes in COVID-19 patients. Last, evidence was presented that targeting platelet P2Y12 represents a promising candidate to reduce proinflammatory platelet-endothelial interactions. Together, these findings demonstrate a previously unappreciated role for platelets and their activation-induced endotheliopathy in COVID-19.

Reference

https://www.science.org/doi/10.1126/sciadv.abh2434

Publication Date: Sep 07, 2021

Functional comparison of MERS-coronavirus lineages reveals increased replicative fitness of the recombinant lineage 5

Abstract

Middle East respiratory syndrome coronavirus (MERS-CoV) is enzootic in dromedary camels across the Middle East and Africa. Virus-induced pneumonia in humans results from animal contact, with a potential for limited onward transmission. Phenotypic changes have been suspected after a novel recombinant clade (lineage 5) caused large nosocomial outbreaks in Saudi Arabia and South Korea in 2016. However, there has been no functional assessment. Here a comprehensive *in vitro* and *ex vivo* comparison of viruses from parental and recombinant virus lineages (lineage 3, n = 7; lineage 4,

n = 8; lineage 5, n = 9 viruses) was performed from Saudi Arabia, isolated immediately before and after the shift toward lineage 5. Replication of lineage 5 viruses is significantly increased. Transcriptional profiling finds reduced induction of immune genes IFNB1, CCL5, and IFNL1 in lung cells infected with lineage 5 strains. Phenotypic differences may be determined by IFN antagonism based on experiments using IFN receptor knock out and signaling inhibition. Additionally, lineage 5 is more resilient against IFN pre-treatment of Calu-3 cells (ca. 10-fold difference in replication). This phenotypic change associated with lineage 5 has remained undiscovered by viral sequence surveillance, but may be a relevant indicator of pandemic potential.

Reference

https://www.nature.com/articles/s41467-021-25519-1

Implementation of an efficient SARS-CoV-2 specimen pooling strategy for high throughput diagnostic testing

Abstract

The rapid identification and isolation of infected individuals remains a key strategy for controlling the spread of SARS-CoV-2. Frequent testing of populations to detect infection early in asymptomatic or presymptomatic individuals can be a powerful tool for intercepting transmission, especially when the viral prevalence is low. However, RT-PCR testing—the gold standard of SARS-CoV-2 diagnosis—is expensive, making regular testing of every individual unfeasible. Sample pooling is one approach to lowering costs. By combining samples and testing them in groups the number of tests required is reduced, substantially lowering costs. Here it was reported on the implementation of pooling strategies using 3-d and 4-d hypercubes to test a professional sports team in South Africa. It was shown that infected samples can be reliably detected in groups of 27 and 81, with minimal loss of assay sensitivity for samples with individual Ct values of up to 32. It was reported on the automation of sample pooling, using a liquid-handling robot and an automated web interface to identify positive samples. It was concluded that hypercube pooling allows for the reliable RT-PCR detection of SARS-CoV-2 infection, at significantly lower costs than lateral flow antigen (LFA) tests.

Reference

https://www.nature.com/articles/s41598-021-96934-z

C_{60} fullerene against SARS-CoV-2 coronavirus: An *in silico* insight

Abstract

Based on WHO reports the new SARS-CoV-2 coronavirus is currently widespread all over the world. So far > 162 million cases have been confirmed, including > 3 million deaths. Because of the pandemic still spreading across the globe the accomplishment of computational methods to find new potential mechanisms of virus inhibitions is necessary. According to the fact that C_{60} fullerene (a sphere-shaped molecule consisting of carbon) has shown inhibitory activity against various protein targets, here the analysis of the potential binding mechanism between SARS-CoV-2 proteins 3CLpro and RdRp with C_{60} fullerene was done; it has resulted in one and two possible binding mechanisms, respectively. In the case of 3CLpro, C_{60} fullerene interacts in the catalytic binding pocket. And for RdRp in the first model C_{60} fullerene blocks RNA synthesis pore and in the second one it prevents binding with Nsp8 co-factor (without this complex formation, RdRp can't perform its initial functions). Then the molecular dynamics simulation confirmed the stability of created complexes. The obtained results might be a basis for other computational studies of 3CLPro and RdRp potential inhibition ways as well as the potential usage of C_{60} fullerene in the fight against COVID-19 disease.

Reference

https://www.nature.com/articles/s41598-021-97268-6

Dynamics of SARS-CoV-2 mutations reveals regional-specificity and similar trends of N501 and high-frequency mutation N501Y in different levels of control measures

Abstract

Coronavirus disease 2019 (COVID-19) is a contagious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). This disease has spread globally, causing more than 161.5 million cases and 3.3 million deaths to date. Surveillance and monitoring of new mutations in the virus' genome are crucial to our understanding of the

adaptation of SARS-CoV-2. Moreover, how the temporal dynamics of these mutations is influenced by control measures and non-pharmaceutical interventions (NPIs) is poorly understood. Using 1,058,020 SARS-CoV-2 from sequenced COVID-19 cases from 98 countries (totaling 714 country-month combinations), we perform a normalization by COVID-19 cases to calculate the relative frequency of SARS-CoV-2 mutations and explore their dynamics over time. 115 Mutations were found, estimated to be present in more than 3% of global COVID-19 cases and determined three types of mutation dynamics: high-frequency, medium-frequency, and low-frequency. Classification of mutations based on temporal dynamics enable us to examine viral adaptation and evaluate the effects of implemented control measures in virus evolution during the pandemic. It was shown that medium-frequency mutations are characterized by high prevalence in specific regions and/or in constant competition with other mutations in several regions. Finally, taking N501Y mutation as representative of high-frequency mutations, we showed that level of control measure stringency negatively correlates with the effective reproduction number of SARS-CoV-2 with high-frequency or not-high-frequency and both follows similar trends in different levels of stringency.

Reference

https://www.nature.com/articles/s41598-021-97267-7

SARS-CoV2 infection: Functional and morphological cardiopulmonary changes in elite handball players

Abstract

There is increasing evidence of cardiac involvement post-SARS-CoV-2 infections in symptomatic as well as in oligo- and asymptomatic athletes. This study aimed to characterize the possible early effects of SARS-CoV-2 infections on myocardial morphology and cardiopulmonary function in athletes. Eight male elite handball players (27 ± 3.5 y) with past SARS-CoV-2 infection were compared with four uninfected teammates (22 ± 2.6 y). Infected athletes were examined 19 ± 7 days after the first positive PCR test. Echocardiographic assessment of the global longitudinal strain under resting conditions was not significantly changed (-17.7% vs. -18.1%). However, magnetic resonance imaging showed minor signs of acute inflammation/oedema in all infected athletes (T2-mapping: $+4.1$ ms, $p = 0.034$) without reaching the Lake-Louis

criteria. Spiroergometric analysis showed a significant reduction in VO2max (− 292 ml/min, − 7.0%), oxygen pulse (− 2.4 ml/beat, − 10.4%), and respiratory minute volume (VE) (− 18.9 l/min, − 13.8%) in athletes with a history of SARS-CoV2 infection ($p < 0.05$, respectively). The parameters were unchanged in the uninfected teammates. SARS-CoV2 infection caused impairment of cardiopulmonary performance during physical effort in elite athletes. It seems reasonable to screen athletes after SARS-CoV2 infection with spiroergometry to identify performance limitations and to guide the return to competition.

Reference

https://www.nature.com/articles/s41598-021-97120-x

RBD-homodimer, a COVID-19 subunit vaccine candidate, elicits immunogenicity and protection in rodents and nonhuman primates

Abstract

The pandemic of COVID-19 caused by SARS-CoV-2 has raised new challenges to the scientific and industrious fields after over 1-year spread across different countries. The ultimate approach to end the pandemic is the timely application of vaccines to achieve herd immunity. Here, a novel SARS-CoV-2 receptor-binding domain (RBD) homodimer was developed as a SARS-CoV-2 vaccine candidate. Formulated with aluminum adjuvant, RBD dimer elicited strong immune response in both rodents and non-human primates, and protected mice from SARS-CoV-2 challenge with significantly reducing viral load and alleviating pathological injury in the lung. In the non-human primates, the vaccine could prevent majority of the animals from SARS-CoV-2 infection in the respiratory tract and reduce lung damage. In addition, antibodies elicited by this vaccine candidate showed cross-neutralization activities to SARS-CoV-2 variants. Furthermore, with our expression system, we provided a high-yield RBD homodimer vaccine without additional biosafety or special transport device supports. Thus, it may serve as a safe, effective, and low-cost SARS-CoV-2 vaccine candidate.

Reference

https://www.nature.com/articles/s41421-021-00320-y

A simple method to describe the COVID-19 trajectory and dynamics in any country based on Johnson cumulative density function fitting

Abstract

A simple method is utilised to study and compare COVID-19 infection dynamics between countries based on curve fitting to publicly shared data of confirmed COVID-19 infections. The method was tested using data from 80 countries from 6 continents. It was found that Johnson cumulative density functions (CDFs) were extremely well fitted to the data ($R^2 > 0.99$) and that Johnson CDFs were much better fitted to the tails of the data than either the commonly used normal or lognormal CDFs. Fitted Johnson CDFs can be used to obtain basic parameters of the infection wave, such as the percentage of the population infected during an infection wave, the days of the start, peak and end of the infection wave, and the duration of the wave's increase and decrease. These parameters can be easily interpreted biologically and used both for describing infection wave dynamics and in further statistical analysis. The usefulness of the parameters obtained was analysed with respect to the relation between the gross domestic product (GDP) per capita, the population density, the percentage of the population infected during an infection wave, the starting day and the duration of the infection wave in the 80 countries. It was found that all the above parameters were significantly associated with GDP per capita, but only the percentage of the population infected was significantly associated with population density. If used with caution, this method has a limited ability to predict the future trajectory and parameters of an ongoing infection wave.

Reference

https://www.nature.com/articles/s41598-021-97285-5

Effectiveness of the BNT162b2 mRNA COVID-19 vaccine in pregnancy

Abstract

To evaluate the effectiveness of the BNT162b2 messenger RNA vaccine in pregnant women, an observational cohort study of pregnant women aged 16 years or older, with no history of SARS-CoV-2, was conducted, who were vaccinated between 20 December 2020 and 3 June 2021. A total of 10,861 vaccinated pregnant women were matched to 10,861 unvaccinated pregnant controls using demographic and clinical

characteristics. Study outcomes included documented infection with SARS-CoV-2, symptomatic COVID-19, COVID-19-related hospitalization, severe illness and death. Estimated vaccine effectiveness from 7 through to 56 d after the second dose was 96% (95% confidence interval 89–100%) for any documented infection, 97% (91–100%) for infections with documented symptoms and 89% (43–100%) for COVID-19-related hospitalization. Only one event of severe illness was observed in the unvaccinated group and no deaths were observed in either group. In summary, the BNT162b2 mRNA vaccine was estimated to have high vaccine effectiveness in pregnant women, which is similar to the effectiveness estimated in the general population.

Reference

https://www.nature.com/articles/s41591-021-01490-8

Prevalence of right ventricular dysfunction and impact on all-cause death in hospitalized patients with COVID-19: A systematic review and meta-analysis

Abstract

The Coronavirus Disease (COVID-19) pandemic imposed a high burden of morbidity and mortality. In COVID-19, direct lung parenchymal involvement and pulmonary microcirculation dysfunction may entail pulmonary hypertension (PH). PH and direct cardiac injury beget right ventricular dysfunction (RVD) occurrence, which has been frequently reported in COVID-19 patients; however, the prevalence of RVD and its impact on outcomes during COVID-19 are still unclear. This study aims to evaluate the prevalence of RVD and associated outcomes in patients with COVID-19, through a Systematic Review and Meta-Analysis. MEDLINE and EMBASE were systematically searched from inception to 15th July 2021. All studies reporting either the prevalence of RVD in COVID-19 patients or all-cause death according to RVD status were included. The pooled prevalence of RVD and Odds Ratio (OR) for all-cause death according to RVD status were computed and reported. Subgroup analysis and meta-regression were also performed. Among 29 studies (3813 patients) included, pooled prevalence of RVD was 20.4% (95% CI 17.1–24.3%; 95% PI 7.8–43.9%), with a high grade of heterogeneity. No significant differences were found across geographical locations, or according to the risk of bias. Severity of COVID-19 was associated with increased prevalence of RVD at meta-regression. The presence of RVD was found associated

with an increased likelihood of all-cause death (OR 3.32, 95% CI 1.94–5.70). RVD was found in 1 out of 5 COVID-19 patients, and was associated with all-cause mortality. RVD may represent one crucial marker for prognostic stratification in COVID-19; further prospective and larger are needed to investigate specific management and therapeutic approach for these patients.

Reference

https://www.nature.com/articles/s41598-021-96955-8

Mental and neurological disorders and risk of COVID-19 susceptibility, illness severity and mortality: A systematic review, meta-analysis and call for action

Abstract

Background: Coronavirus disease 2019 (COVID-19) has evolved into a worldwide pandemic, and has been found to be closely associated with mental and neurological disorders. It was aimed to comprehensively quantify the association between mental and neurological disorders, both pre-existing and subsequent, and the risk of susceptibility, severity and mortality of COVID-19.

Methods: In this systematic review and meta-analysis, PubMed, Web of Science, Embase, PsycINFO, and Cochrane library databases were searched for studies published from the inception up to January 16, 2021 and updated at July 7, 2021. Observational studies including cohort and case-control, cross-sectional studies and case series that reported risk estimates of the association between mental or neurological disorders and COVID-19 susceptibility, illness severity and mortality were included. Two researchers independently extracted data and conducted the quality assessment. Based on I2 heterogeneity, a random effects model was used to calculate pooled odds ratios (OR) and 95% confidence intervals (95% CI). Subgroup analyses and meta-regression analysis were also performed. This study was registered on PROSPERO (registration number: CRD 42021230832).

Finding: A total of 149 studies (227,351,954 participants, 89,235,737 COVID-19 patients) were included in this analysis, in which 27 reported morbidity (132,727,798), 56 reported illness severity (83,097,968) and 115 reported mortality (88,878,662). Overall, mental and neurological disorders were associated with a significant high risk of

infection (pre-existing mental: OR 1·67, 95% CI 1·12-2·49; and pre-existing neurological: 2·05, 1·58-2·67), illness severity (mental: pre-existing, 1·40, 1·25-1·57; sequelae, 4·85, 2·53-9·32; neurological: pre-existing, 1·43, 1·09-1·88; sequelae, 2·17, 1·45-3·24), and mortality (mental: pre-existing, 1·47, 1·26-1·72; neurological: pre-existing, 2·08, 1·61-2·69; sequelae, 2·03, 1·66-2·49) from COVID-19. Subgroup analysis revealed that association with illness severity was stronger among younger COVID-19 patients, and those with subsequent mental disorders, living in low- and middle-income regions. Younger patients with mental and neurological disorders were associated with higher mortality than elders. For type-specific mental disorders, susceptibility to contracting COVID-19 was associated with pre-existing mood disorders, anxiety, and attention-deficit hyperactivity disorder (ADHD); illness severity was associated with both pre-existing and subsequent mood disorders as well as sleep disturbance; and mortality was associated with pre-existing schizophrenia. For neurological disorders, susceptibility was associated with pre-existing dementia; both severity and mortality were associated with subsequent delirium and altered mental status; besides, mortality was associated with pre-existing and subsequent dementia and multiple specific neurological diseases. Heterogeneities were substantial across studies in most analysis.

Interpretation: The findings show an important role of mental and neurological disorders in the context of COVID-19 and provide clues and directions for identifying and protecting vulnerable populations in the pandemic. Early detection and intervention for neurological and mental disorders are urgently needed to control morbidity and mortality induced by the COVID-19 pandemic. However, there was substantial heterogeneity among the included studies, and the results should be interpreted with caution. More studies are needed to explore long-term mental and neurological sequela, as well as the underlying brain mechanisms for the sake of elucidating the causal pathways for these associations.

Reference

https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00391-6/fulltext

Humoral and cellular responses to mRNA vaccines against SARS-CoV-2 in patients with a history of CD20 B-cell-depleting therapy (RituxiVac): An investigator-initiated, single-centre, open-label study

Abstract

Background: B-cell-depleting therapies increase the risk of morbidity and mortality due to COVID-19. Evidence-based SARS-CoV-2 vaccination strategies for patients on B-cell-depleting therapies are scarce. It was aimed to investigate humoral and cell-mediated immune responses to SARS-CoV-2 mRNA-based vaccines in patients receiving CD20-targeted B-cell-depleting agents for autoimmune disease, malignancy, or transplantation.

Methods: The RituxiVac study was an investigator-initiated, single-centre, open-label study done at the Bern University Hospital (Bern, Switzerland). Patients with a treatment history of anti-CD20-depleting agents (rituximab or ocrelizumab) and with no previous history of SARS-CoV-2 infection were enrolled between April 26 and June 30, 2021, for analysis of humoral and cell-mediated immune responses (by interferon-γ [IFNγ] release assay) at least 4 weeks after completing vaccination against SARS-CoV-2. Healthy controls without a history of SARS-CoV-2 infection were also enrolled at least 4 weeks after completing vaccination against SARS-CoV-2. All study participants received two doses of either the Pfizer–BioNTech BNT162b2 vaccine or the Moderna mRNA-1273 vaccine. The primary outcome was the proportion of patients with a history of anti-CD20 treatment who showed a humoral immune response against the SARS-CoV-2 spike protein in comparison with immunocompetent controls. Prespecified secondary endpoints were the effect of anti-CD20 therapy (including time since last treatment and cumulative dose) on humoral or cell-mediated immune responses to SARS-CoV-2 vaccination, and biomarkers of immunocompetence. This study is registered with ClinicalTrials.gov, NCT04877496.

Findings: The final study population comprised 96 patients and 29 immunocompetent controls. The median age of patients was 67 years (IQR 57–72) and of controls was 54 years (45–62), and 51 (53%) of 96 patients and 19 (66%) of 29 controls were female. The median time since last anti-CD20 treatment was 1·07 years (IQR 0·48–2·55) and the median cumulative dose of an anti-CD20 depleting agent was 2·80 g (1·50–5·00).

Anti-spike IgG antibodies were detected in 47 (49%) of 96 patients 1·79 months (IQR 1·16–2·48) after the second vaccine dose compared to 29 (100%) of 29 controls 1·81 months (1·17–2·48) after the second vaccine dose (p<0·001). SARS-CoV-2-specific IFNγ release was detected in 13 (20%) of 66 patients and 21 (75%) of 28 of healthy controls (p<0·001). Only nine (14%) of 66 patients were double positive for anti-SARS-CoV-2 spike IgG and cell-mediated responses, compared with 21 (75%) of 28 healthy controls (p<0·001). Time since last anti-CD20 therapy (>7·6 months; positive predictive value 0·78), peripheral CD19+ cell count (>27 cells per µL; positive predictive value 0·70), and CD4+ lymphocyte count (>653 cells per µL; positive predictive value 0·71) were predictive of humoral vaccine response (area under the curve [AUC] 67% [95% CI 56–78] for time since last anti-CD20 therapy, 67% [55–80] for peripheral CD19+ count, and 66% [54–79] for CD4+ count).

Interpretation: This study provides further evidence of blunted humoral and cell-mediated immune responses elicited by SARS-CoV-2 mRNA vaccines in patients with a history of CD20 B-cell-depleting treatment. Lymphocyte subpopulation counts were associated with vaccine response in this highly vulnerable population. On validation, these results could help guide both the administration of SARS-CoV-2 vaccines and B-cell-depleting agents in this population.

Reference

https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(21)00251-4/fulltext

Immunity elicited by natural infection or Ad26.COV2.S vaccination protects hamsters against SARS-CoV-2 variants of concern

Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants of concern have emerged and may pose a threat to both the efficacy of vaccines based on the original WA1/2020 strain as well as to natural immunity induced by infection with earlier SARS-CoV-2 variants. It was investigated how mutations in the spike protein of circulating SARS-CoV-2 variants, which have been shown to partially evade neutralizing antibodies, impact natural and vaccine-induced immunity. A Syrian hamster model of moderate to severe clinical disease for two variant strains of SARS-CoV-2: B.1.1.7 (α variant) and B.1.351 (β variant) was adapted. We then assessed the protective efficacy

conferred by either natural immunity from WA1/2020 infection or by vaccination with a single dose of the adenovirus serotype 26 vaccine, Ad26.COV2.S. Primary infection with the WA1/2020 strain provided potent protection against weight loss and viral replication in lungs following re-challenge with WA1/2020, B.1.1.7, or B.1.351. Ad26.COV2.S induced cross-reactive binding and neutralizing antibodies that were reduced against the B.1.351 strain compared with WA1/2020, but nevertheless still provided robust protection against B.1.351 challenge, as measured by weight loss and pathology scoring in the lungs. Taken together, these data support hamsters as a pre-clinical model to study protection against emerging variants of SARS-CoV-2 conferred by prior infection or vaccination.

Reference

https://www.science.org/doi/10.1126/scitranslmed.abj3789

SARS-CoV-2 B.1.617.2 Delta variant replication and immune evasion

Abstract

The SARS-CoV-2 B.1.617.2 (Delta) variant was first identified in the state of Maharashtra in late 2020 and spread throughout India, outcompeting pre-existing lineages including B.1.617.1 (Kappa) and B.1.1.7 (Alpha). *In vitro*, B.1.617.2 is 6-fold less sensitive to serum neutralising antibodies from recovered individuals, and 8-fold less sensitive to vaccine-elicited antibodies as compared to wild type (WT) Wuhan-1 bearing D614G. Serum neutralising titres against B.1.617.2 were lower in ChAdOx-1 versus BNT162b2 vaccinees. B.1.617.2 spike pseudotyped viruses exhibited compromised sensitivity to monoclonal antibodies against the receptor binding domain (RBD) and N-terminal domain (NTD). B.1.617.2 demonstrated higher replication efficiency in both airway organoid and human airway epithelial systems compared to B.1.1.7, associated with B.1.617.2 spike in a predominantly cleaved state compared to B.1.1.7. The B.1.617.2 spike protein was able to mediate highly efficient syncytium formation that was less sensitive to inhibition by neutralising antibody as compared to WT spike. Additionally it was observed that B.1.617.2 had higher replication and spike mediated entry as compared to B.1.617.1, potentially explaining B.1.617.2 dominance.

In an analysis of over 130 SARS-CoV-2 infected healthcare workers across three centres in India during a period of mixed lineage circulation, reduced ChAdOx-1 vaccine effectiveness against B.1.617.2 relative to non- B.1.617.2 was observed, with the caveat of possible residual confounding. Compromised vaccine efficacy against the highly fit and immune evasive B.1.617.2 Delta variant warrants continued infection control measures in the post-vaccination era.

Reference

https://www.nature.com/articles/s41586-021-03944-y

SARS-CoV-2 crosses the blood–brain barrier accompanied with basement membrane disruption without tight junctions alteration

Abstract

SARS-CoV-2 has been reported to show a capacity for invading the brains of humans and model animals. However, it remains unclear whether and how SARS-CoV-2 crosses the blood–brain barrier (BBB). Herein, SARS-CoV-2 RNA was occasionally detected in the vascular wall and perivascular space, as well as in brain microvascular endothelial cells (BMECs) in the infected K18-hACE2 transgenic mice. Moreover, the permeability of the infected vessel was increased. Furthermore, disintegrity of BBB was discovered in the infected hamsters by administration of Evans blue. Interestingly, the expression of claudin5, ZO-1, occludin and the ultrastructure of tight junctions (TJs) showed unchanged, whereas, the basement membrane was disrupted in the infected animals. Using an *in vitro* BBB model that comprises primary BMECs with astrocytes, SARS-CoV-2 was found to infect and cross through the BMECs. Consistent with *in vivo* experiments, the expression of MMP9 was increased and collagen IV was decreased while the markers for TJs were not altered in the SARS-CoV-2-infected BMECs. Besides, inflammatory responses including vasculitis, glial activation, and upregulated inflammatory factors occurred after SARS-CoV-2 infection. Overall, the results provide evidence supporting that SARS-CoV-2 can cross the BBB in a transcellular pathway accompanied with basement membrane disrupted without obvious alteration of TJs.

Reference

https://www.nature.com/articles/s41392-021-00719-9

Integrated analysis of plasma and single immune cells uncovers metabolic changes in individuals with COVID-19

Abstract

A better understanding of the metabolic alterations in immune cells during severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection may elucidate the wide diversity of clinical symptoms experienced by individuals with coronavirus disease 2019 (COVID-19). Here, the metabolic changes were reported that were associated with the peripheral immune response of 198 individuals with COVID-19 through an integrated analysis of plasma metabolite and protein levels as well as single-cell multiomics analyses from serial blood draws collected during the first week after clinical diagnosis. The emergence of rare but metabolically dominant T cell subpopulations were documented and it was found that increasing disease severity correlates with a bifurcation of monocytes into two metabolically distinct subsets. This integrated analysis reveals a robust interplay between plasma metabolites and cell-type-specific metabolic reprogramming networks that is associated with disease severity and could predict survival.

Reference

https://www.nature.com/articles/s41587-021-01020-4

The emergence and ongoing convergent evolution of the SARS-CoV-2 N501Y lineages

Abstract

The independent emergence late in 2020 of the B.1.1.7, B.1.351 and P.1 lineages of SARS-CoV-2 prompted renewed concerns about the evolutionary capacity of this virus to overcome public health interventions and rising population immunity. Here, by examining patterns of synonymous and non-synonymous mutations that have accumulated in SARS-CoV-2 genomes since the pandemic began, we find that the emergence of these three "501Y lineages" coincided with a major global shift in the selective forces acting on various SARS-CoV-2 genes. Following their emergence, the adaptive evolution of 501Y lineage viruses has involved repeated selectively favoured convergent mutations at 35 genome sites: mutations we refer to as the 501Y meta-

signature. The ongoing convergence of viruses in many other lineages on this meta-signature suggests that it includes multiple mutation combinations capable of promoting the persistence of diverse SARS-CoV-2 lineages in the face of mounting host immune recognition.

Reference

https://www.cell.com/cell/fulltext/S0092-8674(21)01050-3

Assessment of avidity related to IgG subclasses in SARS-CoV-2 Brazilian infected patients

Abstract

SARS-CoV-2 is considered a global emergency, resulting in an exacerbated crisis in the health public in the world. Although there are advances in vaccine development, it is still limited for many countries. On the other hand, an immunological response that mediates protective immunity or indicates that predict disease outcome in SARS-CoV-2 infection remains undefined. This work aimed to assess the antibody levels, avidity, and subclasses of IgG to RBD protein, in symptomatic patients with severe and mild forms of COVID-19 in Brazil using an adapted in-house RBD-IgG ELISA. The RBD IgG-ELISA showed 100% of specificity and 94.3% of sensibility on detecting antibodies in the sera of hospitalized patients. Patients who presented severe COVID-19 had higher anti-RBD IgG levels compared to patients with mild disease. Additionally, most patients analyzed displayed low antibody avidity, with 64.4% of the samples of patients who recovered from the disease and 84.6% of those who died in this avidity range. The data also reveals an increase of IgG1 and IgG3 levels since the 8th day after symptoms onset, while IgG4 levels maintained less detectable during the study period. Surprisingly, patients who died during 8–14 and 15–21 days also showed higher anti-RBD IgG4 levels in comparison with the recovered ($P < 0.05$), suggesting that some life-threatening patients can elicit IgG4 to RBD antibody response in the first weeks of symptoms onset. The findings constitute the effort to clarify IgG antibodies' kinetics, avidity, and subclasses against SARS-CoV-2 RBD in symptomatic patients with COVID-19 in Brazil, highlighting the importance of IgG antibody avidity in association with IgG4

detection as tool laboratory in the follow-up of hospitalized patients with more significant potential for life-threatening.

Reference

https://www.nature.com/articles/s41598-021-95045-z

Early treatment of COVID-19 with anakinra guided by soluble urokinase plasminogen receptor plasma levels: A double-blind, randomized controlled phase 3 trial

Abstract

Early increase of soluble urokinase plasminogen activator receptor (suPAR) serum levels is indicative of increased risk of progression of coronavirus disease 2019 (COVID-19) to respiratory failure. The SAVE-MORE double-blind, randomized controlled trial evaluated the efficacy and safety of anakinra, an IL-1α/β inhibitor, in 594 patients with COVID-19 at risk of progressing to respiratory failure as identified by plasma suPAR ≥6 ng ml−1, 85.9% (n = 510) of whom were receiving dexamethasone. At day 28, the adjusted proportional odds of having a worse clinical status (assessed by the 11-point World Health Organization Clinical Progression Scale (WHO-CPS)) with anakinra, as compared to placebo, was 0.36 (95% confidence interval 0.26–0.50). The median WHO-CPS decrease on day 28 from baseline in the placebo and anakinra groups was 3 and 4 points, respectively (odds ratio (OR) = 0.40, $P < 0.0001$); the respective median decrease of Sequential Organ Failure Assessment (SOFA) score on day 7 from baseline was 0 and 1 points (OR = 0.63, $P = 0.004$). Twenty-eight-day mortality decreased (hazard ratio = 0.45, $P = 0.045$), and hospital stay was shorter.

Reference

https://www.nature.com/articles/s41591-021-01499-z

Ascorbic acid as an adjunctive therapy in critically ill patients with COVID-19: A propensity score matched study

Abstract

Ascorbic acid represents an appealing option for clinicians to utilize in the context of the global COVID-19 pandemic due to its proposed clinical efficacy, relative safety, and low

cost. The aim of this study was to evaluate the efficacy and safety of using ascorbic acid in supplemental doses as adjunctive therapy for patients critically ill with COVID-19. This was a two-center, non-interventional, retrospective cohort study. All critically ill adult patients admitted to ICU with a confirmed COVID-19 diagnosis between March 1st and December 31st, 2020, were included in the final analysis. The study was conducted at two large governmental tertiary hospitals in Saudi Arabia. The purpose was to investigate the clinical outcomes of low-dose ascorbic acid as adjunctive therapy in COVID-19 after propensity score matching using baseline severity scores, systematic use of corticosteroids, and study centers. A number of 739 patients were included in this study, among whom 296 patients were included after propensity score matching. There was no association between the administration of ascorbic acid and in-hospital mortality or the 30-day mortality [OR (95% CI) 0.77 (0.47, 1.23), p value = 0.27 and OR (95% CI) 0.73 (0.43, 1.20), p value = 0.21, respectively]. Using ascorbic acid was associated with a lower incidence of thrombosis compared with the non-ascorbic-acid group [6.1% vs. 13% respectively; OR (95% CI) 0.42 (0.184, 0.937), p value = 0.03]. Low dose of ascorbic acid as an adjunctive therapy in COVID-19 critically ill patients was not associated with mortality benefits, but it was associated with a lower incidence of thrombosis. Further studies are required to confirm these findings.

Reference

https://www.nature.com/articles/s41598-021-96703-y

Early IFN-α signatures and persistent dysfunction are distinguishing features of NK cells in severe COVID-19

Abstract

Longitudinal analyses of the innate immune system including earliest time points are essential to understand the immunopathogenesis and clinical course of COVID-19. Here, a detailed characterization of natural killer cells were performed in 205 patients (403 samples, day 2-41 after symptom onset) from four independent cohorts using single-cell transcriptomics and proteomics together with functional studies. We found elevated IFN-α plasma levels in early severe COVD-19 alongside increased NK cell expression of ISGs and genes involved in IFN-α signaling, while upregulation of TNF-induced genes was observed in moderate disease. NK cells exert anti-SARS-CoV-2

activity but are functionally impaired in severe COVID-19. Further, NK cell dysfunction may be relevant for development of fibrotic lung disease in severe COVID-19, as NK cells exhibited impaired anti-fibrotic activity. The study indicates preferential IFN-α and TNF responses in severe and moderate COVID-19, respectively, and associates prolonged IFN-α-induced NK cell response with poorer disease outcome.

Reference

https://www.cell.com/immunity/fulltext/S1074-7613(21)00365-4

Emerging SARS-CoV-2 variants of concern evade humoral immune responses from infection and vaccination

Abstract

Emerging SARS-CoV-2 variants of concern (VOCs) pose a threat to human immunity induced by natural infection and vaccination. The recognition of three VOCs (B.1.1.7, B.1.351, and P.1) was assessed in cohorts of COVID-19 convalescent patients (n = 69) and Pfizer-BioNTech vaccine recipients (n = 50). Spike binding and neutralization against all three VOCs were substantially reduced in most individuals, with the largest four- to sevenfold reduction in neutralization being observed against B.1.351. While hospitalized patients with COVID-19 and vaccinees maintained sufficient neutralizing titers against all three VOCs, 39% of nonhospitalized patients exhibited no detectable neutralization against B.1.351. Moreover, monoclonal neutralizing antibodies show sharp reductions in their binding kinetics and neutralizing potential to B.1.351 and P.1 but not to B.1.1.7. These data have implications for the degree to which pre-existing immunity can protect against subsequent infection with VOCs and informs policy makers of susceptibility to globally circulating SARS-CoV-2 VOCs.

Reference

https://www.science.org/doi/10.1126/sciadv.abj5365

Increased vulnerability to SARS-CoV-2 infection among indigenous people living in the urban area of Manaus

Abstract

The COVID-19 pandemic threatens indigenous peoples living in suburban areas of large Brazilian cities and has thus far intensified their pre-existing socio-economic inequalities. It was evaluated the epidemiological situation of SARS-CoV-2 infection among residents of the biggest urban multiethnic indigenous community of the Amazonas state, Brazil. Blood samples of 280 indigenous people living in the surrounding area of Manaus were tested for the presence of anti-SARS-CoV-2 IgA or IgG antibodies. The risk factors and sociodemographic information were assessed through an epidemiological questionnaire. It was found that a total positivity rate of 64.64% (95% CI 59.01–70.28) for SARS-CoV-2 infection. IgA and IgG were detected in 55.71% (95% CI 49.89–61.54) and 60.71% (95% CI 54.98–66.45) of the individuals, respectively. Over 80% of positive individuals were positive for both IgA and IgG.No significant difference in positivity rates between genders or age groups was observed. Moreover, the age group ≥ 60 years old showed the highest antibody ratios (IgA mean ratio = 3.080 ± 1.623; IgG mean ratio = 4.221 ± 1.832), while the age groups 13–19 and 20–29 showed the lowest IgA (mean ratio = 2.268 ± 0.919) and IgG ratios (mean ratio = 2.207 ± 1.246), respectively. Individuals leaving the home more frequently were at higher risk of infection (Odds ratio (OD) 2.61; 95% CI 1.00–1.49; p = 0.048). Five or more individuals per household increased fivefold the risk of virus transmission (OR 2.56; 95% CI 1.09–6.01; p = 0.019). The disproportionate dissemination of SARS-CoV-2 infection observed among the study population might be driven by typical cultural behavior and socioeconomic inequalities. Despite the pandemic threat, this population is not being targeted by public policies and appears to be chronically invisible to the Brazilian authorities.

Reference

https://www.nature.com/articles/s41598-021-96843-1

Mental well-being during the first months of Covid-19 in adults and children: Behavioral evidence and neural precursors

Abstract

Pandemics such as the Covid-19 pandemic have shown to impact our physical and mental well-being, with particular challenges for children and families. We describe data from 43 adults (31♀, ages = 22–51; 21 mothers) and 26 children (10♀, ages = 7–17 years) including pre-pandemic brain function and seven assessment points during the first months of the pandemic. It was investigated that (1) changes in child and adult well-being, (2) mother–child associations of mental well-being, and (3) associations between pre-pandemic brain activation during mentalizing and later fears or burden. In adults the prevalence of clinically significant anxiety-levels was 34.88% and subthreshold depression 32.56%. Caregiver burden in parents was moderately elevated. Overall, scores of depression, anxiety, and caregiver burden decreased across the 11 weeks after Covid-19-onset. Children's behavioral and emotional problems during Covid-19 did not significantly differ from pre-pandemic levels and decreased during restrictions. Mothers' subjective burden of care was associated with children's emotional and behavioral problems, while depression levels in mothers were related to children's mood. Furthermore, meeting friends was a significant predictor of children's mood during early restrictions. Pre-pandemic neural correlates of mentalizing in prefrontal regions preceded later development of fear of illnesses and viruses in all participants, while temporoparietal activation preceded higher subjective burden in mothers.

Reference

https://www.nature.com/articles/s41598-021-96852-0

The relationship between serum 25-hydroxyvitamin D levels and the severity of COVID-19 disease and its mortality

Abstract

Supplemental vitamin D can reduce the risk and mortality of viral pneumonia. The relationship between 25 hydroxyvitamin D [25(OH)D] levels and the severity and mortality of Coronavirus disease 2019 (COVID-19) was evaluated. In this cross-sectional study, the admitted patients with COVID-19 were categorized as mild,

moderate, severe, and critical based on clinical and radiologic characteristics. Calcium, phosphorus, albumin, creatinine, and serum 25(OH)D were measured and their correlation with the severity of disease and mortality were analyzed. During 2 months, 508 patients (442 patients in general wards and 66 patients in the intensive care unit (ICU)) were included. The participants were 56 ± 17 years old (52% male, 37% with comorbidity). Concerning severity, 13%, 42%, 36%, and 9% had mild, moderate, severe, and critical diseases, respectively. The mortality rate was 10.8%. Admission to ICU, severity of disease and mortality decreased significantly across quartiles of 25(OH)D. According to multivariate logistic regression analysis, disease mortality had a positive correlation with age and had a negative correlation with the serum level of 25(OH)D, calcium, and albumin. In hospitalized patients with COVID-19, low 25(OH)D was associated with severe disease and increased ICU admission and mortality rate.

Reference

https://www.nature.com/articles/s41598-021-97017-9

Racial and ethnic disparity in clinical outcomes among patients with confirmed COVID-19 infection in a large US electronic health record database

Abstract

Background: Racial and ethnic minority groups have been disproportionately affected by the US coronavirus disease 2019 (COVID-19) pandemic; however, nationwide data on COVID-19 outcomes stratified by race/ethnicity and adjusted for clinical characteristics are sparse. This study analyzed the impacts of race/ethnicity on outcomes among US patients with COVID-19.

Methods: This was a retrospective observational study of patients with a confirmed COVID-19 diagnosis in the electronic health record from 01 February 2020 through 14 September 2020. Index encounter site, hospitalization, and mortality were assessed by race/ethnicity (Hispanic, non-Hispanic Black [Black], non-Hispanic White [White], non-Hispanic Asian [Asian], or Other/unknown). Associations between racial/ethnic categories and study outcomes adjusted for patient characteristics were evaluated using logistic regression.

Findings: Among 202,908 patients with confirmed COVID-19, patients from racial/ethnic minority groups were more likely than White patients to be hospitalized on initial presentation (Hispanic: adjusted odds ratio 1·690, 95% CI 1·620–1·763; Black: 1·810, 1·743–1·880; Asian: 1·503, 1·381–1·636) and during follow-up (Hispanic: 1·700, 1·638–1·764; Black: 1·578, 1·526–1·633; Asian: 1·391, 1·288–1·501). Among hospitalized patients, adjusted mortality risk was lower for Black patients (0·881, 0·809–0·959) but higher for Asian patients (1·205, 1·000–1·452).

Interpretation: Racial/ethnic minority patients with COVID-19 had more severe disease on initial presentation than White patients. Increased mortality risk was attenuated by hospitalization among Black patients but not Asian patients, indicating that outcome disparities may be mediated by distinct factors for different groups. In addition to enacting policies to facilitate equitable access to COVID-19–related care, further analyses of disaggregated population-level COVID-19 data are needed.

Reference

https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00355-2/fulltext

Adaptive immune determinants of viral clearance and protection in mouse models of SARS-CoV-2

Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has caused more than 160 million infections and more than 3 million deaths worldwide. While effective vaccines are currently being deployed, the adaptive immune determinants that promote viral clearance and confer protection remain poorly defined. Using mouse models of SARS-CoV-2, it was demonstrated that both humoral and cellular adaptive immunity contribute to viral clearance in the setting of primary infection. Furthermore, it was found that either convalescent mice or mice that receive mRNA vaccination are protected from both homologous infection and infection with a variant of concern, B.1.351. Additionally, we find this protection largely mediated by antibody response and not cellular immunity. These results highlight the *in vivo* protective capacity of antibodies generated to both vaccine and natural infection.

Reference

PERSPECTIVE

Mesenchymal stem cell therapy for severe COVID-19

The coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has placed a global public burden on health authorities. Although the virological characteristics and pathogenesis of COVID-19 has been largely clarified, there is currently no specific therapeutic measure. In severe cases, acute SARS-CoV-2 infection leads to immune disorders and damage to both the adaptive and innate immune responses. Having roles in immune regulation and regeneration, mesenchymal stem cells (MSCs) serving as a therapeutic option may regulate the over-activated inflammatory response and promote recovery of lung damage. Since the outbreak of the COVID-19 pandemic, a series of MSC-therapy clinical trials has been conducted. The findings indicate that MSC treatment not only significantly reduces lung damage, but also improves patient recovery with safety and good immune tolerance. Herein, the recent progress in MSC therapy for COVID-19 was summarized and also highlighted the challenges in the field. For more details, read the link given below.

Reference

https://www.nature.com/articles/s41392-021-00754-6

COMMENT

T cell-oriented strategies for controlling the COVID-19 pandemic

COVID-19 vaccination programmes are ongoing worldwide. Neutralizing antibodies are thought to be key for host protection against COVID-19; however, strategies that focus only on neutralizing antibodies may not be sufficient to cope with the pandemic in the longer term owing to the decay of antibody titres and the emergence of antibody-escape variants of SARS-CoV-2. Here, the protective roles of T cells in COVID-19 were described and the conservation of T cell epitopes in SARS-CoV-2 variants of concern, and discuss the potential contribution of T cell-oriented strategies to controlling the COVID-19 pandemic. For more details, read the link given below.

Reference

https://www.nature.com/articles/s41577-021-00625-9

FORUM

SARS-CoV-2 viral RNA levels are not "viral load"

Efforts Ct values are commonly used as proxies of SARS-CoV-2 "viral load". Since coronaviruses are positive single stranded RNA ((+)ssRNA) viruses, current RT-qPCR target amplification does not distinguish replicative from transcriptional RNA. Although analyses of Ct values remain informative, equating them with viral load may lead to flawed conclusions as it is presently unknown whether (and to what extent) variation in Ct reflects variation in viral load or in gene expression. For more details, read the link given below.

Reference

https://www.cell.com/trends/microbiology/fulltext/S0966-842X(21)00208-0

OPINION

Superspreading in the emergency of COVID-19 variants

Superspreading and Variants of Concern (VOC) of the human pathogen, Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are the main catalyzers of the coronavirus disease 2019 (COVID-19) pandemic. Measuring their individual impact is however, challenging. By examining the largest database of SARS-CoV-2 genomes The Global Initiative on Sharing Avian Influenza Data (GISAID; n > 1.2M high quality sequences), evidence was presented, suggesting that superspreading has played a key role in the epidemiological predominance of VOC. There are clear signatures in the database compatible with large superspreading events coinciding chronologically with the worst epidemiological scenarios triggered by VOC. The data suggest that, without the randomness effect of the genetic drift facilitated by superspreading, new VOC of SARS-CoV-2 would have had more limited chance of success. For more details, read the link given below.

Reference

https://www.cell.com/trends/genetics/fulltext/S0168-9525(21)00262-6