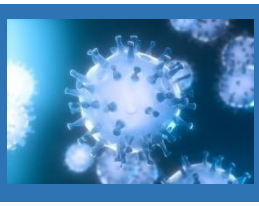

RESEARCH PUBLICATIONS

Publication Date: Jan 13, 2021

Artificial intelligence matches subjective severity assessment of pneumonia for prediction of patient outcome and need for mechanical ventilation: A cohort study

Abstract

To compare the performance of artificial intelligence (AI) and Radiographic Assessment of Lung Edema (RALE) scores from frontal chest radiographs (CXRs) for predicting patient outcomes and the need for mechanical ventilation in COVID-19 pneumonia. The IRB-approved study included 1367 serial CXRs from 405 adult patients (mean age 65 ± 16 years) from two sites in the US (Site A) and South Korea (Site B). Information pertaining to patient demographics (age, gender), smoking history, comorbid conditions (such as cancer, cardiovascular and other diseases), vital signs (temperature, oxygen saturation), and available laboratory data (such as WBC count and CRP) was recorded. Two thoracic radiologists performed the qualitative assessment of all CXRs based on the RALE score for assessing the severity of lung involvement. All CXRs were processed with a commercial AI algorithm to obtain the percentage of the lung affected with findings related to COVID-19 (AI score). Independent t- and chi-square tests were used in addition to multiple logistic regression with Area Under the Curve (AUC) as output for predicting disease outcome and the need for mechanical ventilation. The RALE and AI scores had a strong positive correlation in CXRs from each site ($r2 = 0.79–0.86$; $p < 0.0001$). Patients who died or received mechanical ventilation had significantly higher RALE and AI scores than those with recovery or without the need for mechanical ventilation ($p < 0.001$). Patients with a more substantial difference in baseline and maximum RALE scores and AI scores had a higher prevalence of death and mechanical ventilation ($p < 0.001$). The addition of patients' age, gender, WBC count,

and peripheral oxygen saturation increased the outcome prediction from 0.87 to 0.94 (95% CI 0.90–0.97) for RALE scores and from 0.82 to 0.91 (95% CI 0.87–0.95) for the AI scores. AI algorithm is as robust a predictor of adverse patient outcome (death or need for mechanical ventilation) as subjective RALE scores in patients with COVID-19 pneumonia.

Reference

https://www.nature.com/articles/s41598-020-79470-0

The role of organizational characteristics on the outcome of COVID-19 patients admitted to the ICU in Belgium

Abstract

Background: Several studies have investigated the predictors of in-hospital mortality for COVID-19 patients who need to be admitted to the Intensive Care Unit (ICU). However, no data on the role of organizational issues on patients' outcome are available in this setting. The aim of this study was therefore to assess the role of surge capacity organisation on the outcome of critically ill COVID-19 patients admitted to ICUs in Belgium.

Methods: A retrospective analysis of in-hospital mortality was conducted in Belgian ICU COVID-19 patients *via* the national surveillance database. Non-survivors at hospital discharge were compared to survivors using multivariable mixed effects logistic regression analysis. Specific analyses including only patients with invasive ventilation were performed. To assess surge capacity, data were merged with administrative information on the type of hospital, the baseline number of recognized ICU beds, the number of supplementary beds specifically created for COVID-19 ICU care and the "ICU overflow" (i.e. a time-varying ratio between the number of occupied ICU beds by confirmed and suspected COVID-19 patients divided by the number of recognized ICU beds reserved for COVID-19 patients; ICU overflow was present when this ratio is ≥ 1.0).

Findings: Over a total of 13,612 hospitalised COVID-19 patients with admission and discharge forms registered in the surveillance period (March, 1 to August, 9 2020), 1903 (14.0%) required ICU admission, of whom 1747 had available outcome data. Non-

survivors (n = 632, 36.1%) were older and had more frequently various comorbid diseases than survivors. In the multivariable analysis, ICU overflow, together with older age, presence of comorbidities, shorter delay between symptom onset and hospital admission, absence of hydroxychloroquine therapy and use of invasive mechanical ventilation and of ECMO, was independently associated with an increased in-hospital mortality. Similar results were found in in in the subgroup of invasively ventilated patients. In addition, the proportion of supplementary beds specifically created for COVID-19 ICU care to the previously existing total number of ICU beds was associated with increased in-hospital mortality among invasively ventilated patients. The model also indicated a significant between-hospital difference in in-hospital mortality, not explained by the available patients and hospital characteristics.

Interpretation: Surge capacity organisation as reflected by ICU overflow or the creation of COVID-19 specific supplementary ICU beds were found to negatively impact ICU patient outcomes.

Reference

https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762(20)30019-3/fulltext

Newborn bloodspot screening in the time of COVID-19

Abstract

Purpose: A COVID-19 pandemic business continuity plan (BCP) was rapidly developed to protect the Victorian newborn screening (NBS) program. Here, the outcomes of COVID-19 BCP and its impact on the Victorian NBS laboratory service were present.

Methods: Change management principles were used to develop a BCP that included mapping of NBS processes against staff resources, triaging priorities, technology solutions, supply chain continuity, gap analysis, and supporting maternity service providers. The effect was assessed quantitatively by review of key performance indicator data and qualitatively from staff feedback.

Results: A four-stage BCP was implemented. Stage 1 split teams into two, which rotated weekly, onsite (laboratory) and offsite (home). At 20 weeks post-implementation the BCP only progressed to stage 1 and the overall turnaround time was maintained.

Staff experience indicated benefits from the review of workflow but noted some social impact associated with the change.

Conclusion: The preparedness and agility of implementation was based on our focus on the newborn babies and their families, our production system, and a continuous improvement mindset. Both our people and technology infrastructure processes are crucial to this success as we continue to adapt to new challenges.

Reference

https://www.nature.com/articles/s41436-020-01086-6

Delayed discharge is associated with higher complement C3 levels and a longer nucleic acid-negative conversion time in patients with COVID-19

Abstract

To determine factors associated with delayed discharge of hospitalized patients with coronavirus disease (COVID-19). This retrospective cohort study included 47 patients with COVID-19 admitted to three hospitals in Quanzhou City, Fujian Province, China, between January 21, 2020 and March 6, 2020. Univariate and multivariate logistic regression analyses were conducted to identify factors associated with delayed discharge. The median length of hospital stay was 22 days. Patients in the delayed discharge group (length of hospital stay ≥ 21 days, $n = 27$) were more likely to have diarrhea, anorexia, decreased white blood cell counts, increased complement C3 and C-reactive protein levels, air bronchograms, undergo thymalfasin treatment, and take significantly longer to convert to a severe acute respiratory syndrome coronavirus (SARS-CoV-2) RNA-negative status than those in the control group (length of hospital stay, < 21 days; $n = 20$). In multivariate logistic regression analysis, the time to SARS-CoV-2 RNA-negative conversion (odds ratio [OR]: 1.48, 95% confidence interval [CI] 1.09–2.04, $P = 0.01$) and complement C3 levels (OR 1.14 95% CI 1.02–1.27, $P = 0.03$) were the only risk factors independently associated with delayed discharge from the hospital. Dynamic monitoring of complement C3 and SARS-CoV-2 RNA levels is useful for predicting delayed discharge of patients.

Reference

https://www.nature.com/articles/s41598-021-81010-3

Corticosteroid treatment has no effect on hospital mortality in COVID-19 patients

Abstract

Since the start of the novel coronavirus 2019 (COVID-19) pandemic, corticosteroid use has been the subject of debate. The available evidence is uncertain, and knowledge on the subject is evolving. The aim of the cohort study was to evaluate the association between corticosteroid therapy and hospital mortality, in patients hospitalized with COVID-19 after balancing for possible confounders. One thousand four hundred forty four patients were admitted to our hospital with a positive RT-PCR test for SARS-CoV-2, 559 patients (39%) were exposed to corticosteroids during hospital stay, 844 (61%) were not exposed to corticosteroids. In the cohort of patients exposed to corticosteroids, 171 (30.6%) died. In the cohort of patients not exposed to corticosteroids, 183 (21.7%) died (unadjusted $p < 0.001$). Nonetheless, exposure to corticosteroids was not associated with in-hospital mortality after balancing with overlap weight propensity score (adjusted $p = 0.25$). Patients in the corticosteroids cohort had a reduced risk of ICU admission (adjusted $p < 0.001$). Treatment with corticosteroids did not affect hospital mortality in patients with COVID-19 after balancing for confounders. A possible advantage of corticosteroid therapy was to reduce Intensive Care Unit admission, which could be useful in reducing pressure on Intensive Care Units in times of limited resources, as during the COVID-19 pandemic.

Reference

https://www.nature.com/articles/s41598-020-80654-x

Competing-risk analysis of coronavirus disease 2019 in-hospital mortality in a Northern Italian centre from SMAtteo COvid19 REgistry (SMACORE)

Abstract

An accurate prediction of the clinical outcomes of European patients requiring hospitalisation for Coronavirus Disease 2019 (COVID-19) is lacking. The aim of the study is to identify predictors of in-hospital mortality and discharge in a cohort of Lombardy patients with COVID-19. All consecutive hospitalised patients from February

21st to March 30th, 2020, with confirmed COVID-19 from the IRCCS Policlinico San Matteo, Pavia, Lombardy, Italy, were included. In-hospital mortality and discharge were evaluated by competing risk analysis. The Fine and Gray model was fitted in order to estimate the effect of covariates on the cumulative incidence functions (CIFs) for in-hospital mortality and discharge. 426 adult patients [median age 68 (IQR 56 to 77 years)] were admitted with confirmed COVID-19 over a 5-week period; 292 (69%) were male. By 21 April 2020, 141 (33%) of these patients had died, 239 (56%) patients had been discharged and 46 (11%) were still hospitalised. Among these 46 patients, updated as of 30 May, 2020, 5 (10.9%) had died, 8 (17.4%) were still in ICU, 12 (26.1%) were transferred to lower intensity care units and 21 (45.7%) were discharged. Regression on the CIFs for in-hospital mortality showed that older age, male sex, number of comorbidities and hospital admission after March 4th were independent risk factors associated with in-hospital mortality. Older age, male sex and number of comorbidities definitively predicted in-hospital mortality in hospitalised patients with COVID-19.

Reference

https://www.nature.com/articles/s41598-020-80679-2

Ontological modeling and analysis of experimentally or clinically verified drugs against coronavirus infection

Abstract

Our systematic literature collection and annotation identified 106 chemical drugs and 31 antibodies effective against the infection of at least one human coronavirus (including SARS-CoV, SAR-CoV-2, and MERS-CoV) in vitro or in vivo in an experimental or clinical setting. A total of 163 drug protein targets were identified, and 125 biological processes involving the drug targets were significantly enriched based on a Gene Ontology (GO) enrichment analysis. The Coronavirus Infectious Disease Ontology (CIDO) was used as an ontological platform to represent the anti-coronaviral drugs, chemical compounds, drug targets, biological processes, viruses, and the relations among these entities. In addition to new term generation, CIDO also adopted various terms from existing ontologies and developed new relations and axioms to semantically represent our annotated knowledge. The CIDO knowledgebase was systematically

analyzed for scientific insights. To support rational drug design, a “Host-coronavirus interaction (HCI) checkpoint cocktail” strategy was proposed to interrupt the important checkpoints in the dynamic HCI network, and ontologies would greatly support the design process with interoperable knowledge representation and reasoning.

Reference

https://www.nature.com/articles/s41597-021-00799-w

Stability of SARS-CoV-2 on critical personal protective equipment

Abstract

The spread of COVID-19 in healthcare settings is concerning, with healthcare workers representing a disproportionately high percentage of confirmed cases. Although SARS-CoV-2 virus has been found to persist on surfaces for a number of days, the extent and duration of fomites as a mode of transmission, particularly in healthcare settings, has not been fully characterized. To shed light on this critical matter, the present study provides the first comprehensive assessment of SARS-CoV-2 stability on experimentally contaminated personal protective equipment (PPE) widely used by healthcare workers and the general public. Persistence of viable virus was monitored over 21 days on eight different materials, including nitrile medical examination gloves, reinforced chemical resistant gloves, N-95 and N-100 particulate respirator masks, Tyvek, plastic, cotton, and stainless steel. Unlike previous reports, viable SARS-CoV-2 in the presence of a soil load persisted for up to 21 days on experimentally inoculated PPE, including materials from filtering facepiece respirators (N-95 and N-100 masks) and a plastic visor. Conversely, when applied to 100% cotton fabric, the virus underwent rapid degradation and became undetectable by TCID50 assay within 24 h. These findings underline the importance of appropriate handling of contaminated PPE during and following use in high-risk settings and provide interesting insight into the potential utility of cotton in limiting COVID-19 transmission.

Reference

https://www.nature.com/articles/s41598-020-80098-3

A therapeutic neutralizing antibody targeting receptor binding domain of SARS-CoV-2 spike protein

Abstract

Vaccines and therapeutics are urgently needed for the pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Here, we screen human monoclonal antibodies (mAb) targeting the receptor binding domain (RBD) of the viral spike protein via antibody library constructed from peripheral blood mononuclear cells of a convalescent patient. The CT-P59 mAb potently neutralizes SARS-CoV-2 isolates including the D614G variant without antibody-dependent enhancement effect. Complex crystal structure of CT-P59 Fab/RBD shows that CT-P59 blocks interaction regions of RBD for angiotensin converting enzyme 2 (ACE2) receptor with an orientation that is notably different from previously reported RBD-targeting mAbs. Furthermore, therapeutic effects of CT-P59 are evaluated in three animal models (ferret, hamster, and rhesus monkey), demonstrating a substantial reduction in viral titer along with alleviation of clinical symptoms. Therefore, CT-P59 may be a promising therapeutic candidate for COVID-19.

Reference

https://www.nature.com/articles/s41467-020-20602-5

Structure-guided multivalent nanobodies block SARS-CoV-2 infection and suppress mutational escape

Abstract

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic continues to spread with devastating consequences. For passive immunization efforts, nanobodies have size and cost advantages over conventional antibodies. Here, four neutralizing nanobodies were generated that target the receptor-binding domain of the SARS-CoV-2 spike protein. Two distinct binding epitopes were defined using x-ray crystallography and cryo-electron microscopy. Based on the structures, we engineered multivalent nanobodies with more than 100-fold improved neutralizing activity than monovalent nanobodies. Biparatopic nanobody fusions suppressed the emergence of

escape mutants. Several nanobody constructs neutralized through receptor-binding competition, while other monovalent and biparatopic nanobodies triggered aberrant activation of the spike fusion machinery. These premature conformational changes in the spike protein forestalled productive fusion, and rendered the virions non-infectious.

Reference

https://science.sciencemag.org/content/early/2021/01/11/science.abe6230

Mechanism of SARS-CoV-2 polymerase stalling by remdesivir

Abstract

Remdesivir is the only FDA-approved drug for the treatment of COVID-19 patients. The active form of remdesivir acts as a nucleoside analog and inhibits the RNA-dependent RNA polymerase (RdRp) of coronaviruses including SARS-CoV-2. Remdesivir is incorporated by the RdRp into the growing RNA product and allows for addition of three more nucleotides before RNA synthesis stalls. Here we use synthetic RNA chemistry, biochemistry and cryo-electron microscopy to establish the molecular mechanism of remdesivir-induced RdRp stalling. We show that addition of the fourth nucleotide following remdesivir incorporation into the RNA product is impaired by a barrier to further RNA translocation. This translocation barrier causes retention of the RNA 3'-nucleotide in the substrate-binding site of the RdRp and interferes with entry of the next nucleoside triphosphate, thereby stalling RdRp. In the structure of the remdesivir-stalled state, the 3'-nucleotide of the RNA product is matched and located with the template base in the active center, and this may impair proofreading by the viral 3'-exonuclease. These mechanistic insights should facilitate the quest for improved antivirals that target coronavirus replication.

Reference

https://www.nature.com/articles/s41467-020-20542-0

Capsid-like particles decorated with the SARS-CoV-2 receptor-binding domain elicit strong virus neutralization activity

Abstract

The rapid development of a SARS-CoV-2 vaccine is a global priority. Here, two capsid-like particle (CLP)-based vaccines were developed displaying the receptor-binding domain (RBD) of the SARS-CoV-2 spike protein. RBD antigens are displayed on AP205 CLPs through a split-protein Tag/Catcher, ensuring unidirectional and high-density display of RBD. Both soluble recombinant RBD and RBD displayed on CLPs bind the ACE2 receptor with nanomolar affinity. Mice are vaccinated with soluble RBD or CLP-displayed RBD, formulated in Squalene-Water-Emulsion. The RBD-CLP vaccines induce higher levels of serum anti-spike antibodies than the soluble RBD vaccines. Remarkably, one injection with our lead RBD-CLP vaccine in mice elicits virus neutralization antibody titers comparable to those found in patients that had recovered from COVID-19. Following booster vaccinations, the virus neutralization titers exceed those measured after natural infection, at serum dilutions above 1:10,000. Thus, the RBD-CLP vaccine is a highly promising candidate for preventing COVID-19.

Reference

https://www.nature.com/articles/s41467-020-20251-8

Estimating internationally imported cases during the early COVID-19 pandemic

Abstract

Early in the COVID-19 pandemic, predictions of international outbreaks were largely based on imported cases from Wuhan, China, potentially missing imports from other cities. A method was provide, combining daily COVID-19 prevalence and flight passenger volume, to estimate importations from 18 Chinese cities to 43 international destinations, including 26 in Africa. Global case importations from China in early January came primarily from Wuhan, but the inferred source shifted to other cities in mid-February, especially for importations to African destinations. It is estimated that 10.4 (6.2 – 27.1) COVID-19 cases were imported to these African destinations, which exhibited marked variation in their magnitude and main sources of importation. It is estimated that 90% of imported cases arrived between 17 January and 7 February, prior

to the first case detections. The results highlight the dynamic role of source locations, which can help focus surveillance and response efforts.

Reference

https://www.nature.com/articles/s41467-020-20219-8

MDA5 governs the innate immune response to SARS-CoV-2 in lung epithelial cells

Abstract

Recent studies have profiled the innate immune signatures in patients infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and suggest that cellular responses to viral challenge may affect disease severity. Yet the molecular events that underlie cellular recognition and response to SARS-CoV-2 infection remain to be elucidated. Here, we find that SARS-CoV-2 replication induces a delayed interferon (IFN) response in lung epithelial cells. By screening 16 putative sensors involved in sensing of RNA virus infection, we found that MDA5 and LGP2 primarily regulate IFN induction in response to SARS-CoV-2 infection. Further analyses revealed that viral intermediates specifically activate the IFN response through MDA5-mediated sensing. Additionally, we find that IRF3, IRF5, and NF-κB/p65 are the key transcription factors regulating the IFN response during SARS-CoV-2 infection. In summary, these findings provide critical insights into the molecular basis of the innate immune recognition and signaling response to SARS-CoV-2.

Reference

https://www.cell.com/cell-reports/fulltext/S2211-1247(20)31617-X

Enhancement versus neutralization by SARS-CoV-2 antibodies from A convalescent donor associates with distinct epitopes on the receptor-binding domain

Abstract

Several potent neutralizing antibodies against SARS-CoV-2 virus have been identified. However, antibody-dependent enhancement (ADE) has not been comprehensively studied for SARS-CoV-2, and the relationship between enhancing versus neutralizing

activities and antibody epitopes remains unknown. Here, we select a convalescent individual with potent IgG neutralizing activity and characterize his antibody response. Monoclonal antibodies isolated from memory B cells target four groups of five non-overlapping receptor-binding domain (RBD) epitopes. Antibodies to one group of these RBD epitopes mediate ADE of entry in Raji cells via an Fcγ receptor-dependent mechanism. In contrast, antibodies targeting two other distinct epitope groups neutralize SARS-CoV-2 without ADE, while antibodies against the fourth epitope group are poorly neutralizing. One antibody, XG014, potently cross-neutralizes SARS-CoV-2 variants as well as SARS-CoV-1 with respective IC_{50} values as low as 5.1 ng/ml and 23.7 ng/ml, while not exhibiting ADE. Therefore, neutralization and ADE of human SARS-CoV-2 antibodies correlate with non-overlapping RBD epitopes.

Reference

https://www.cell.com/cell-reports/fulltext/S2211-1247(21)00012-7

Publication Date: Jan 11, 2021

Circuits between infected macrophages and T cells in SARS-CoV-2 pneumonia

Abstract

Some patients infected with Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) develop severe pneumonia and the acute respiratory distress syndrome (ARDS). Distinct clinical features in these patients have led to speculation that the immune response to virus in the SARS-CoV-2-infected alveolus differs from other types of pneumonia. Bronchoalveolar lavage fluid samples were collected from 88 patients with SARS-CoV-2-induced respiratory failure and 211 patients with known or suspected pneumonia from other pathogens and subjected them to flow cytometry and bulk transcriptomic profiling. We performed single-cell RNA-seq on 10 bronchoalveolar lavage fluid samples collected from patients with severe COVID-19 within 48 hours of intubation. In the majority of patients with SARS-CoV-2 infection, the alveolar space was persistently enriched in T cells and monocytes. Bulk and single-cell transcriptomic profiling suggested that SARS-CoV-2 infects alveolar macrophages, which in turn respond by producing T cell chemoattractants. These T cells produce interferon-gamma to induce inflammatory cytokine release from alveolar macrophages and further

promote T cell activation. Collectively, our results suggest that SARS-CoV-2 causes a slowly unfolding, spatially limited alveolitis in which alveolar macrophages harboring SARS-CoV-2 and T cells form a positive feedback loop that drives persistent alveolar inflammation.

Reference

https://www.nature.com/articles/s41586-020-03148-w

In silico **validation of potent phytochemical Orientin as inhibitor of SARS-CoV-2 spike and host cell receptor GRP78 binding**

Abstract

The present wellbeing worry to the whole world is the outbreak of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), also called COVID-19. This global health crisis first appeared in Wuhan, China around December 2019 and due to its extremely contagious nature it had spread to almost 187 countries. Still now no effective method of treatment or vaccine is developed for controlling the disease. Therefore, the sole obliging strategy is to take precautionary measures by repurposing drugs from the pre-existing library of therapeutically potent molecules. In this situation of pandemic this repurposing technique may save the labour-intensive and tiresome process of new drug development. Orientin is a natural flavonoid with several beneficial effects. This phytochemical can be isolated from different plants like tulsi or holy basil, black bamboo, passion flowers etc. and it's antiviral, anti-inflammation, vasodilatation and cardioprotective, radioprotective, neuroprotective, anticarcinogeneic and antinociceptive effects are already established. In this research, it is intriguing to find out whether this molecule can interfere the interaction of SARS-CoV-2 spike glycoprotein and their host receptor GRP78. Our in silico docking and molecular dynamics simulation results indicate the binding of Orientin in the overlapping residues of GRP78 binding region of SARS-CoV-2 spike model and SARS-CoV-2 spike model binding region of GRP78 substrate-binding domain. Therefore, the results included in this research work provide a strong possibility of using Orientin as a promising precautionary or therapeutic measure for COVID-19.

Reference

https://www.cell.com/heliyon/fulltext/S2405-8440(21)00028-1

Adaptive immunity to SARS-CoV-2 and COVID-19

Abstract

The adaptive immune system is important for control of most viral infections. The three fundamental components of the adaptive immune system are B cells (the source of antibodies), CD4+ T cells, and CD8+ T cells. The armamentarium of B cells, CD4+ T cells, and CD8+ T cells has differing roles in different viral infections, and in vaccines, and thus it is critical to directly study adaptive immunity to SARS-CoV-2 to understand COVID-19. Knowledge is now available on relationships between antigen-specific immune responses and SARS-CoV-2 infection. While more studies are needed, a picture has begun to emerge that reveals that CD4+ T cells, CD8+ T cells, and neutralizing antibodies all contribute to control of SARS-CoV-2, in both non-hospitalized and hospitalized cases of COVID-19. The specific functions and kinetics of these adaptive immune responses are discussed, as well as their interplay with innate immunity and implications for COVID-19 vaccines and immune memory against re-infection.

Reference

https://www.cell.com/cell/fulltext/S0092-8674(21)00007-6

Stabilizing the closed SARS-CoV-2 spike trimer

Abstract

The trimeric spike (S) protein of SARS-CoV-2 is the primary focus of most vaccine design and development efforts. Due to intrinsic instability typical of class I fusion proteins, S tends to prematurely refold to the post-fusion conformation, compromising immunogenic properties and prefusion trimer yields. To support ongoing vaccine development efforts, we report the structure-based design of soluble S trimers with increased yields and stabilities, based on introduction of single point mutations and disulfide-bridges. We identify regions critical for stability: the heptad repeat region 1, the SD1 domain and position 614 in SD2. We combine a minimal selection of mostly interprotomeric mutations to create a stable S-closed variant with a 6.4-fold higher

expression than the parental construct while no longer containing a heterologous trimerization domain. The cryo-EM structure reveals a correctly folded, predominantly closed pre-fusion conformation. Highly stable and well producing S protein and the increased understanding of S protein structure will support vaccine development and serological diagnostics.

Reference

https://www.nature.com/articles/s41467-020-20321-x

Antibody neutralization of SARS-CoV-2 through ACE2 receptor mimicry

Abstract

Understanding the mechanism for antibody neutralization of SARS-CoV-2 is critical for the development of effective therapeutics and vaccines. A large number of monoclonal antibodies were recently isolated from SARS-CoV-2 infected individuals. Here we select the top three most potent yet variable neutralizing antibodies for in-depth structural and functional analyses. Crystal structural comparisons reveal differences in the angles of approach to the receptor binding domain (RBD), the size of the buried surface areas, and the key binding residues on the RBD of the viral spike glycoprotein. One antibody, P2C-1F11, most closely mimics binding of receptor ACE2, displays the most potent neutralizing activity in vitro and conferred strong protection against SARS-CoV-2 infection in Ad5-hACE2-sensitized mice. It also occupies the largest binding surface and demonstrates the highest binding affinity to RBD. More interestingly, P2C-1F11 triggers rapid and extensive shedding of S1 from the cell-surface expressed spike glycoprotein, with only minimal such effect by the remaining two antibodies. These results offer a structural and functional basis for potent neutralization via disruption of the very first and critical steps for SARS-CoV-2 cell entry.

Reference

https://www.nature.com/articles/s41467-020-20501-9

Optimizing respiratory virus surveillance networks using uncertainty propagation

Abstract

Infectious disease prevention, control and forecasting rely on sentinel observations; however, many locations lack the capacity for routine surveillance. Here it was shown that, by using data from multiple sites collectively, accurate estimation and forecasting of respiratory diseases for locations without surveillance is feasible. A framework was developed to optimize surveillance sites that suppresses uncertainty propagation in a networked disease transmission model. Using influenza outbreaks from 35 US states, the optimized system generates better near-term predictions than alternate systems designed using population and human mobility. It was also found that monitoring regional population centers serves as a reasonable proxy for the optimized network and could direct surveillance for diseases with limited records. The proxy method is validated using model simulations for 3,108 US counties and historical data for two other respiratory pathogens – human metapneumovirus and seasonal coronavirus – from 35 US states and can be used to guide systemic allocation of surveillance efforts.

Reference

https://www.nature.com/articles/s41467-020-20399-3

Isolation of MERS-related coronavirus from lesser bamboo bats that uses DPP4 and infects human-DPP4-transgenic mice

Abstract

While a number of human coronaviruses are believed to be originated from ancestral viruses in bats, it remains unclear if bat coronaviruses are ready to cause direct bat-to-human transmission. Here, the isolation of a MERS-related coronavirus, Tylonycteris-bat-CoV-HKU4, was reported from lesser bamboo bats. Tylonycteris-bat-CoV-HKU4 replicates efficiently in human colorectal adenocarcinoma and hepatocarcinoma cells with cytopathic effects, and can utilize human-dipeptidyl-peptidase-4 and dromedary camel-dipeptidyl-peptidase-4 as the receptors for cell entry. Flow cytometry, co-immunoprecipitation and surface plasmon resonance assays show that Tylonycteris-bat-CoV-HKU4-receptor-binding-domain can bind human-dipeptidyl-peptidase-4, dromedary camel-dipeptidyl-peptidase-4, and Tylonycteris pachypus-dipeptidyl-

peptidase-4. Tylonycteris-bat-CoV-HKU4 can infect human-dipeptidyl-peptidase-4-transgenic mice by intranasal inoculation with self-limiting disease. Positive virus and inflammatory changes were detected in lungs and brains of infected mice, associated with suppression of antiviral cytokines and activation of proinflammatory cytokines and chemokines. The results suggest that MERS-related bat coronaviruses may overcome species barrier by utilizing dipeptidyl-peptidase-4 and potentially emerge in humans by direct bat-to-human transmission.

Reference

https://www.nature.com/articles/s41467-020-20458-9

Duration and key determinants of infectious virus shedding in hospitalized patients with coronavirus disease-2019 (COVID-19)

Abstract

Key questions in COVID-19 are the duration and determinants of infectious virus shedding. Here, we report that infectious virus shedding is detected by virus cultures in 23 of the 129 patients (17.8%) hospitalized with COVID-19. The median duration of shedding infectious virus is 8 days post onset of symptoms (IQR 5–11) and drops below 5% after 15.2 days post onset of symptoms (95% confidence interval (CI) 13.4–17.2). Multivariate analyses identify viral loads above 7 log10 RNA copies/mL (odds ratio [OR] of 14.7 (CI 3.57-58.1; $p < 0.001$) as independently associated with isolation of infectious SARS-CoV-2 from the respiratory tract. A serum neutralizing antibody titre of at least 1:20 (OR of 0.01 (CI 0.003-0.08; $p < 0.001$) is independently associated with non-infectious SARS-CoV-2. We conclude that quantitative viral RNA load assays and serological assays could be used in test-based strategies to discontinue or de-escalate infection prevention and control precautions.

Reference

https://www.nature.com/articles/s41467-020-20568-4

A novel deep learning-based quantification of serial chest computed tomography in Coronavirus Disease 2019 (COVID-19)

Abstract

This study aims to explore and compare a novel deep learning-based quantification with the conventional semi-quantitative computed tomography (CT) scoring for the serial chest CT scans of COVID-19. 95 patients with confirmed COVID-19 and a total of 465 serial chest CT scans were involved, including 61 moderate patients (moderate group, 319 chest CT scans) and 34 severe patients (severe group, 146 chest CT scans). Conventional CT scoring and deep learning-based quantification were performed for all chest CT scans for two study goals: (1) Correlation between these two estimations; (2) Exploring the dynamic patterns using these two estimations between moderate and severe groups. The Spearman's correlation coefficient between these two estimation methods was 0.920 ($p < 0.001$). predicted pulmonary involvement (CT score and percent of pulmonary lesions calculated using deep learning-based quantification) increased more rapidly and reached a higher peak on 23rd days from symptom onset in severe group, which reached a peak on 18th days in moderate group with faster absorption of the lesions. The deep learning-based quantification for COVID-19 showed a good correlation with the conventional CT scoring and demonstrated a potential benefit in the estimation of disease severities of COVID-19.

Reference

https://www.nature.com/articles/s41598-020-80261-w

A trimeric human angiotensin-converting enzyme 2 as an anti-SARS-CoV-2 agent

Abstract

Effective intervention strategies are urgently needed to control the COVID-19 pandemic. Human angiotensin-converting enzyme 2 (ACE2) is a membrane-bound carboxypeptidase that forms a dimer and serves as the cellular receptor for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). ACE2 is also a key negative regulator of the renin–angiotensin system that modulates vascular functions. We report here the properties of a trimeric ACE2 ectodomain variant, engineered using a structure-based approach. The trimeric ACE2 variant has a binding affinity of ~60 pM for

the spike protein of SARS-CoV-2 (compared with 77 nM for monomeric ACE2 and 12–22 nM for dimeric ACE2 constructs), and its peptidase activity and the ability to block activation of angiotensin II receptor type 1 in the renin–angiotensin system are preserved. Moreover, the engineered ACE2 potently inhibits SARS-CoV-2 infection in cell culture. These results suggest that engineered, trimeric ACE2 may be a promising anti-SARS-CoV-2 agent for treating COVID-19.

Reference

https://www.nature.com/articles/s41594-020-00549-3

No evidence for basigin/CD147 as a direct SARS-CoV-2 spike binding receptor

Abstract

The spike protein of SARS-CoV-2 is known to enable viral invasion into human cells through direct binding to host receptors including ACE2. An alternate entry receptor for the virus was recently proposed to be basigin/CD147. These early studies have already prompted a clinical trial and multiple published hypotheses speculating on the role of this host receptor in viral infection and pathogenesis. Here, it was reported that it was not capable to find evidence supporting the role of basigin as a putative spike binding receptor. Recombinant forms of the SARS-CoV-2 spike do not interact with basigin expressed on the surface of human cells, and by using specialized assays tailored to detect receptor interactions as weak or weaker than the proposed basigin-spike binding, we report no evidence for a direct interaction between the viral spike protein to either of the two common isoforms of basigin. Finally, removing basigin from the surface of human lung epithelial cells by CRISPR/Cas9 results in no change in their susceptibility to SARS-CoV-2 infection. Given the pressing need for clarity on which viral targets may lead to promising therapeutics, these findings were present to allow more informed decisions about the translational relevance of this putative mechanism in the race to understand and treat COVID-19.

Reference

https://www.nature.com/articles/s41598-020-80464-1

A novel ACE2 isoform is expressed in human respiratory epithelia and is upregulated in response to interferons and RNA respiratory virus infection

Abstract

Angiotensin-converting enzyme 2 (ACE2) is the main entry point in airway epithelial cells for SARS-CoV-2. ACE2 binding to the SARS-CoV-2 protein spike triggers viral fusion with the cell plasma membrane, resulting in viral RNA genome delivery into the host. Despite ACE2's critical role in SARS-CoV-2 infection, full understanding of ACE2 expression, including in response to viral infection, remains unclear. ACE2 was thought to encode five transcripts and one protein of 805 amino acids. In the present study, we identify a novel short isoform of ACE2 expressed in the airway epithelium, the main site of SARS-CoV-2 infection. Short ACE2 is substantially upregulated in response to interferon stimulation and rhinovirus infection, but not SARS-CoV-2 infection. This short isoform lacks SARS-CoV-2 spike high-affinity binding sites and, altogether, our data are consistent with a model where short ACE2 is unlikely to directly contribute to host susceptibility to SARS-CoV-2 infection.

Reference

https://www.nature.com/articles/s41588-020-00759-x

Development and structural basis of a two-MAb cocktail for treating SARS-CoV-2 infections

Abstract

The ongoing pandemic of coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Neutralizing antibodies against SARS-CoV-2 are an option for drug development for treating COVID-19. Here, the identification and characterization of two groups were reported of mouse neutralizing monoclonal antibodies (MAbs) targeting the receptor-binding domain (RBD) on the SARS-CoV-2 spike (S) protein. MAbs 2H2 and 3C1, representing the two antibody groups, respectively, bind distinct epitopes and are compatible in formulating a noncompeting antibody cocktail. A humanized version of the 2H2/3C1 cocktail is found to potently neutralize authentic SARS-CoV-2 infection in vitro with half inhibitory concentration (IC50) of 12 ng/mL and effectively treat SARS-CoV-2-infected mice even

when administered at as late as 24 h post-infection. We determine an ensemble of cryo-EM structures of 2H2 or 3C1 Fab in complex with the S trimer up to 3.8 Å resolution, revealing the conformational space of the antigen–antibody complexes and MAb-triggered stepwise allosteric rearrangements of the S trimer, delineating a previously uncharacterized dynamic process of coordinated binding of neutralizing antibodies to the trimeric S protein. The findings provide important information for the development of MAb-based drugs for preventing and treating SARS-CoV-2 infections.

Reference

https://www.nature.com/articles/s41467-020-20465-w

Development and validation of the ISARIC 4C Deterioration model for adults hospitalised with COVID-19: A prospective cohort study

Abstract

Background: Prognostic models to predict the risk of clinical deterioration in acute COVID-19 cases are urgently required to inform clinical management decisions.

Methods: A multivariable logistic regression model for in-hospital clinical deterioration (defined as any requirement of ventilatory support or critical care, or death) was developed and validated among consecutively hospitalised adults with highly suspected or confirmed COVID-19 who were prospectively recruited to the International Severe Acute Respiratory and Emerging Infections Consortium Coronavirus Clinical Characterisation Consortium (ISARIC4C) study across 260 hospitals in England, Scotland, and Wales. Candidate predictors that were specified a priori were considered for inclusion in the model on the basis of previous prognostic scores and emerging literature describing routinely measured biomarkers associated with COVID-19 prognosis. Internal–external cross-validation was used to evaluate discrimination, calibration, and clinical utility across eight National Health Service (NHS) regions in the development cohort. It was further validated the final model in held-out data from an additional NHS region (London).

Findings: 74 944 participants (recruited between Feb 6 and Aug 26, 2020) were included, of whom 31 924 (43·2%) of 73 948 with available outcomes met the composite clinical deterioration outcome. In internal–external cross-validation in the

development cohort of 66 705 participants, the selected model (comprising 11 predictors routinely measured at the point of hospital admission) showed consistent discrimination, calibration, and clinical utility across all eight NHS regions. In held-out data from London (n=8239), the model showed a similarly consistent performance (C-statistic 0·77 [95% CI 0·76 to 0·78]; calibration-in-the-large 0·00 [–0·05 to 0·05]); calibration slope 0·96 [0·91 to 1·01]), and greater net benefit than any other reproducible prognostic model.

Interpretation: The 4C Deterioration model has strong potential for clinical utility and generalisability to predict clinical deterioration and inform decision making among adults hospitalised with COVID-19.

Reference

https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30559-2/fulltext

Publication Date: Jan 09, 2021

Multi-organ proteomic landscape of COVID-19 autopsies

Abstract

The molecular pathology of multi-organ injuries in COVID-19 patients remains unclear, preventing effective therapeutics development. Here, we report a proteomic analysis of 144 autopsy samples from seven organs in 19 COVID-19 patients. 11,394 Proteins in these samples were quantified, in which 5336 were perturbed in the COVID-19 patients compared to controls. Our data showed that cathepsin L1, rather than ACE2, was significantly upregulated in the lung from the COVID-19 patients. Systemic hyperinflammation and dysregulation of glucose and fatty acid metabolism were detected in multiple organs. We also observed dysregulation of key factors involved in hypoxia, angiogenesis, blood coagulation and fibrosis in multiple organs from the COVID-19 patients. Evidence for testicular injuries include reduced Leydig cells, suppressed cholesterol biosynthesis and sperm mobility. In summary, this study depicts a multi-organ proteomic landscape of COVID-19 autopsies that furthers our understanding of the biological basis of COVID-19 pathology.

Reference

https://www.cell.com/cell/fulltext/S0092-8674(21)00004-0

Publication Date: Jan 08, 2021

Prevalence and risk factors for delirium in critically ill patients with COVID-19 (COVID-D): A multicentre cohort study

Abstract

Background: To date, 750 000 patients with COVID-19 worldwide have required mechanical ventilation and thus are at high risk of acute brain dysfunction (coma and delirium). It was aimed to investigate the prevalence of delirium and coma, and risk factors for delirium in critically ill patients with COVID-19, to aid the development of strategies to mitigate delirium and associated sequelae.

Methods: This multicentre cohort study included 69 adult intensive care units (ICUs), across 14 countries. We included all patients (aged ≥18 years) admitted to participating ICUs with severe acute respiratory syndrome coronavirus 2 infection before April 28, 2020. Patients who were moribund or had life-support measures withdrawn within 24 h of ICU admission, prisoners, patients with pre-existing mental illness, neurodegenerative disorders, congenital or acquired brain damage, hepatic coma, drug overdose, suicide attempt, or those who were blind or deaf were excluded. We collected de-identified data from electronic health records on patient demographics, delirium and coma assessments, and management strategies for a 21-day period. Additional data on ventilator support, ICU length of stay, and vital status was collected for a 28-day period. The primary outcome was to determine the prevalence of delirium and coma and to investigate any associated risk factors associated with development of delirium the next day. We also investigated predictors of number of days alive without delirium or coma. These outcomes were investigated using multivariable regression.

Findings: Between Jan 20 and April 28, 2020, 4530 patients with COVID-19 were admitted to 69 ICUs, of whom 2088 patients were included in the study cohort. The median age of patients was 64 years (IQR 54 to 71) with a median Simplified Acute Physiology Score (SAPS) II of 40·0 (30·0 to 53·0). 1397 (66·9%) of 2088 patients were invasively mechanically ventilated on the day of ICU admission and 1827 (87·5%) were

invasively mechanical ventilated at some point during hospitalisation. Infusion with sedatives while on mechanical ventilation was common: 1337 (64·0%) of 2088 patients were given benzodiazepines for a median of 7·0 days (4·0 to 12·0) and 1481 (70·9%) were given propofol for a median of 7·0 days (4·0 to 11·0). Median Richmond Agitation–Sedation Scale score while on invasive mechanical ventilation was –4 (–5 to –3). 1704 (81·6%) of 2088 patients were comatose for a median of 10·0 days (6·0 to 15·0) and 1147 (54·9%) were delirious for a median of 3·0 days (2·0 to 6·0). Mechanical ventilation, use of restraints, and benzodiazepine, opioid, and vasopressor infusions, and antipsychotics were each associated with a higher risk of delirium the next day (all $p \leq 0{\cdot}04$), whereas family visitation (in person or virtual) was associated with a lower risk of delirium ($p < 0{\cdot}0001$). During the 21-day study period, patients were alive without delirium or coma for a median of 5·0 days (0·0 to 14·0). At baseline, older age, higher SAPS II scores, male sex, smoking or alcohol abuse, use of vasopressors on day 1, and invasive mechanical ventilation on day 1 were independently associated with fewer days alive and free of delirium and coma (all $p < 0{\cdot}01$). 601 (28·8%) of 2088 patients died within 28 days of admission, with most of those deaths occurring in the ICU.

Interpretation: Acute brain dysfunction was highly prevalent and prolonged in critically ill patients with COVID-19. Benzodiazepine use and lack of family visitation were identified as modifiable risk factors for delirium, and thus these data present an opportunity to reduce acute brain dysfunction in patients with COVID-19.

Reference

https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30552-X/fulltext#%20

Immunogenicity and protective efficacy of BBV152, whole virion inactivated SARS- CoV-2 vaccine candidates in the Syrian hamster model

Abstract

The availability of a safe and effective vaccine would be the eventual measure to deal with SARS-CoV-2 threat. Here, the immunogenicity and protective efficacy of inactivated SARS-CoV-2 vaccine candidates BBV152A, BBV152B and BBV152C have been assessed in Syrian hamsters. Three dose vaccination regimes with vaccine candidates induced significant titres of SARS-CoV-2 specific IgG and neutralizing

antibodies. BBV152A and BBV152B vaccine candidates remarkably generated a quick and robust immune response. Post-SARS-CoV-2 infection, vaccinated hamsters did not show any histopathological changes in the lungs. The protection of the hamster was evident by the rapid clearance of the virus from lower respiratory tract, reduced virus load in upper respiratory tract, absence of lung pathology and robust humoral immune response. These findings confirm the immunogenic potential of the vaccine candidates and further protection of hamsters challenged with SARS-CoV-2. Out of the three candidates, BBV152A showed the better response.

Reference

https://www.cell.com/iscience/fulltext/S2589-0042(21)00022-5

A high-throughput liquid bead-array assay confirms strong correlation between SARS-CoV-2 antibody level and COVID-19 severity

Abstract

A detailed understanding of the adaptive host response to SARS-CoV-2 infection in humans is urgently needed. a sensitive, high-throughput, and efficient assay was developed using liquid bead array technology. Advantages over traditional ELISA were observed for the detection and quantification of binding IgG against the receptor binding domain (RBD) of SARS-CoV-2. To determine whether COVID-19 symptom severity correlates with SARS-CoV-2 IgG, anti-RBD IgG levels were measured from 67 subjects recovered from PCR-confirmed COVID-19. It was found that COVID-19 symptom severity strongly correlated with RBD IgG level ($p<0.001$). These findings have substantial implications for public policy surrounding assessments of antibody responses and possible immunity, as not all cases of COVID-19 can be assumed to generate a protective antibody response, and mild disease in particular is capable of generating very low-level anti-RBD IgG levels. These findings also have important implications for the selection of donors for convalescent plasma to be used therapeutically.

Reference

https://www.cell.com/iscience/fulltext/S2589-0042(21)00020-1

“It seems like COVID-19 now is the only disease present on Earth”: Living with a rare or undiagnosed disease during the COVID-19 pandemic

Abstract

Purpose: Patients with rare and undiagnosed diseases (RUDs) face significant health challenges, which may be exacerbated during the COVID-19 pandemic. The goal of this study was to identify specific impacts of the pandemic on RUD patients, and targets for improving support and health-care access.

Methods: An online survey was conducted of RUD patients and their family members from 21 April to 8 June 2020, recruited from 76 Facebook groups for RUDs. Questions assessed patient characteristics and impacts of the pandemic on RUD diagnosis and management.

Results: Respondents (n = 413), including 274 RUD patients and 139 family members, were predominantly female and white, though income varied. Impacts of the pandemic included (1) barriers to accessing essential health care, (2) specific impacts of restrictive COVID-19 visitation policies on ability to advocate in health-care settings, (3) uncertainty and fear regarding COVID-19 risk, (4) exacerbated physical and mental health challenges, (5) magnified impacts of reduced educational and therapeutic services, and (6) unexpected positive changes due to the pandemic.

Conclusion: There are specific, serious challenges affecting RUD patients and families during the COVID-19 pandemic. There is an urgent need to develop approaches to mitigate these challenges both during and beyond the pandemic.

Reference

https://www.nature.com/articles/s41436-020-01069-7

AXL is a candidate receptor for SARS-CoV-2 that promotes infection of pulmonary and bronchial epithelial cells

Abstract

The current coronavirus disease 2019 (COVID-19) pandemic presents a global public health challenge. The viral pathogen responsible, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), binds to the host receptor ACE2 through its spike (S)

glycoprotein, which mediates membrane fusion and viral entry. Although the role of ACE2 as a receptor for SARS-CoV-2 is clear, studies have shown that ACE2 expression is extremely low in various human tissues, especially in the respiratory tract. Thus, other host receptors and/or co-receptors that promote the entry of SARS-CoV-2 into cells of the respiratory system may exist. In this study, we found that the tyrosine-protein kinase receptor UFO (AXL) specifically interacts with the N-terminal domain of SARS-CoV-2 S. Using both a SARS-CoV-2 virus pseudotype and authentic SARS-CoV-2, we found that overexpression of AXL in HEK293T cells promotes SARS-CoV-2 entry as efficiently as overexpression of ACE2, while knocking out AXL significantly reduces SARS-CoV-2 infection in H1299 pulmonary cells and in human primary lung epithelial cells. Soluble human recombinant AXL blocks SARS-CoV-2 infection in cells expressing high levels of AXL. The AXL expression level is well correlated with SARS-CoV-2 S level in bronchoalveolar lavage fluid cells from COVID-19 patients. Taken together, our findings suggest that AXL is a novel candidate receptor for SARS-CoV-2 which may play an important role in promoting viral infection of the human respiratory system and indicate that it is a potential target for future clinical intervention strategies.

Reference

https://www.nature.com/articles/s41422-020-00460-y

ABBV-744 as a potential inhibitor of SARS-CoV-2 main protease enzyme against COVID-19

Abstract

A new pathogen severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has spread worldwide and become pandemic with thousands new deaths and infected cases globally. To address coronavirus disease (COVID-19), currently no effective drug or vaccine is available. This necessity motivated us to explore potential lead compounds by considering drug repurposing approach targeting main protease (M^{pro}) enzyme of SARS-CoV-2. This enzyme considered to be an attractive drug target as it contributes significantly in mediating viral replication and transcription. Herein, comprehensive computational investigations were performed to identify potential inhibitors of SARS-CoV-2 M^{pro} enzyme. The structure-based pharmacophore modeling was developed based on the co-crystallized structure of the enzyme with its biological active inhibitor.

The generated hypotheses were applied for virtual screening based PhaseScore. Docking based virtual screening workflow was used to generate hit compounds using HTVS, SP and XP based Glide GScore. The pharmacological and physicochemical properties of the selected lead compounds were characterized using ADMET. Molecular dynamics simulations were performed to explore the binding affinities of the considered lead compounds. Binding energies revealed that compound ABBV-744 binds to the M^{pro} with strong affinity (ΔG_{bind} −45.43 kcal/mol), and the complex is more stable in comparison with other protein–ligand complexes. Our study classified three best compounds which could be considered as promising inhibitors against main protease SARS-CoV-2 virus.

Reference

https://www.nature.com/articles/s41598-020-79918-3

Host and viral determinants for efficient SARS-CoV-2 infection of the human lung

Abstract

Understanding the factors that contribute to efficient SARS-CoV-2 infection of human cells may provide insights on SARS-CoV-2 transmissibility and pathogenesis, and reveal targets of intervention. Here, host and viral determinants were analyzed, which were essential for efficient SARS-CoV-2 infection in both human lung epithelial cells and ex vivo human lung tissues. It was identified that heparan sulfate as an important attachment factor for SARS-CoV-2 infection. Next, it was shown that sialic acids present on ACE2 prevent efficient spike/ACE2-interaction. While SARS-CoV infection is substantially limited by the sialic acid-mediated restriction in both human lung epithelial cells and ex vivo human lung tissues, infection by SARS-CoV-2 is limited to a lesser extent. It was further demonstrated that the furin-like cleavage site in SARS-CoV-2 spike is required for efficient virus replication in human lung but not intestinal tissues. These findings provide insights on the efficient SARS-CoV-2 infection of human lungs.

Reference

https://www.nature.com/articles/s41467-020-20457-w

Host mitochondrial transcriptome response to SARS-CoV-2 in multiple cell models and clinical samples

Abstract

SARS-CoV-2 induces a muted innate immune response compared to other respiratory viruses. Mitochondrial dynamics might partially mediate this effect of SARS-CoV-2 on innate immunity. Polypeptides encoded by open reading frames of SARS-CoV and SARS-CoV-2 have been shown to localize to mitochondria and disrupt Mitochondrial Antiviral Signaling (MAVS) protein signaling. Therefore, we hypothesized that SARS-CoV-2 would distinctly regulate the mitochondrial transcriptome. It was analyzed multiple publicly available RNASeq data derived from primary cells, cell lines, and clinical samples (i.e., BALF and lung). It was reported that SARS-CoV-2 did not dramatically regulate (1) mtDNA-encoded gene expression or (2) MAVS expression, and (3) SARS-CoV-2 downregulated nuclear-encoded mitochondrial (NEM) genes related to cellular respiration and Complex I.

Reference

https://www.nature.com/articles/s41598-020-79552-z

Publication Date: Jan 07, 2021

High mortality rate in COVID-19 patients with myeloproliferative neoplasms after abrupt withdrawal of ruxolitinib

Abstract

The clinical presentation and risk factors were reported for survival in 175 patients with myeloproliferative neoplasms (MPN) and COVID-19, diagnosed between February and June 2020. After a median follow-up of 50 days, mortality was higher than in the general population and reached 48% in myelofibrosis (MF). Univariate analysis, showed a significant relationship between death and age, male gender, decreased lymphocyte counts, need for respiratory support, comorbidities and diagnosis of MF, while no association with essential thrombocythemia (ET), polycythemia vera (PV), and prefibrotic-PMF (pre-PMF) was found. Regarding MPN-directed therapy ongoing at the time of COVID-19 diagnosis, Ruxolitinib (Ruxo) was significantly more frequent in patients who died in comparison with survivors ($p = 0.006$). Conversely, multivariable

analysis found no effect of Ruxo alone on mortality, but highlighted an increased risk of death in the 11 out of 45 patients who discontinued treatment. These findings were also confirmed in a propensity score matching analysis. In conclusion, it was found that a high risk of mortality during COVID-19 infection among MPN patients, especially in MF patients and/or discontinuing Ruxo at COVID-19 diagnosis. These findings call for deeper investigation on the role of Ruxo treatment and its interruption, in affecting mortality in MPN patients with COVID-19.

Reference

https://www.nature.com/articles/s41375-020-01107-y

Development and validation of a risk score using complete blood count to predict in-hospital mortality in COVID-19 patients

Abstract

Objective: To develop a sensitive risk assessment score predicting the risk of mortality in patients with coronavirus disease 2019 (COVID-19) using complete blood count (CBC) during hospitalization.

Methods: A retrospective cohort study was performed from a total of 13,138 in-patients with COVID-19 in Hubei Province, China, and Milan, Italy. Among them, 9,810 with ≥ twice CBC records from Hubei province were assigned to the training cohort. CBC parameters were analyzed as potential predictors for all-cause mortality and were selected by the generalized linear mixed model (GLMM).

Findings: Five risk factors were derived to construct a composite score (PAWNN score) using Cox proportional hazards regression model, including Platelet counts, Age, White blood cell counts, Neutrophil counts, and Neutrophil/lymphocyte ratio. PAWNN score showed good accuracy for predicting mortality in 10-fold cross-validation (AUROCs 0.92-0.93) and subsets with different quartile intervals of follow up and pre-existing diseases. The performance of the score was further validated in 2,949 patients with only one CBC record from Hubei Cohort (AUROC 0.97) and 227 patients from the Italian cohort (AUROC 0.80). The Latent Markov Model (LMM) yielded discernible patient's statuses, among which the PAWNN score was a distinguishing feature. PAWNN score

showed good prediction power for transition probabilities between different latent conditions.

Conclusions: The PAWNN score is a simple and accurate risk assessment tool that can predict the mortality risk for COVID-19 patients during entire hospitalization. This tool can assist clinicians in prioritizing medical treatment of COVID-19 in-patients, particularly in less developed regions with limited resources.

Reference

https://www.cell.com/med/fulltext/S2666-6340(20)30079-9

Continuation *versus* discontinuation of renin–angiotensin system inhibitors in patients admitted to hospital with COVID-19: A prospective, randomised, open-label trial

Abstract

Background: Biological considerations suggest that renin–angiotensin system inhibitors might influence the severity of COVID-19. It was aimed to evaluate whether continuing versus discontinuing renin–angiotensin system inhibitors (angiotensin-converting enzyme inhibitors or angiotensin receptor blockers) affects outcomes in patients admitted to hospital with COVID-19.

Methods: The REPLACE COVID trial was a prospective, randomised, open-label trial done at 20 large referral hospitals in seven countries worldwide. Eligible participants were aged 18 years and older who were admitted to hospital with COVID-19 and were receiving a renin–angiotensin system inhibitor before admission. Individuals with contraindications to continuation or discontinuation of renin–angiotensin system inhibitor therapy were excluded. Participants were randomly assigned (1:1) to continuation or discontinuation of their renin–angiotensin system inhibitor using permuted block randomisation, with allocation concealed using a secure web-based randomisation system. The primary outcome was a global rank score in which participants were ranked across four hierarchical tiers incorporating time to death, duration of mechanical ventilation, time on renal replacement or vasopressor therapy, and multiorgan dysfunction during the hospitalisation. Primary analyses were done in the intention-to-

treat population. The REPLACE COVID trial is registered with ClinicalTrials.gov, NCT04338009.

Findings: Between March 31 and Aug 20, 2020, 152 participants were enrolled and randomly assigned to either continue or discontinue renin–angiotensin system inhibitor therapy (continuation group n=75; discontinuation group n=77). Mean age of participants was 62 years (SD 12), 68 (45%) were female, mean body-mass index was 33 kg/m2 (SD 8), and 79 (52%) had diabetes. Compared with discontinuation of renin–angiotensin system inhibitors, continuation had no effect on the global rank score (median rank 73 [IQR 40–110] for continuation vs 81 [38–117] for discontinuation; β-coefficient 8 [95% CI −13 to 29]). There were 16 (21%) of 75 participants in the continuation arm versus 14 (18%) of 77 in the discontinuation arm who required intensive care unit admission or invasive mechanical ventilation, and 11 (15%) of 75 participants in the continuation group versus ten (13%) of 77 in the discontinuation group died. 29 (39%) participants in the continuation group and 28 (36%) participants in the discontinuation group had at least one adverse event ($\chi 2$ test of adverse events between treatment groups p=0·77). There was no difference in blood pressure, serum potassium, or creatinine during follow-up across the two groups.

Interpretation: Consistent with international society recommendations, renin–angiotensin system inhibitors can be safely continued in patients admitted to hospital with COVID-19.

Reference

https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30558-0/fulltext

SARS-CoV-2: Characterisation and mitigation of risks associated with aerosol generating procedures in dental practices

Abstract

Introduction: The objectives were to characterise the particle size distribution of aerosols generated by standard dental aerosol generating procedures (AGPs) and to assess the impact of aerosol-management interventions on 'fallow time'. Interventions included combinations of high-volume intraoral suction (HVS[IO]), high-volume extraoral suction (HVS[EO]) and an air cleaning system (ACS).

Method: A sequence of six AGPs were performed on a phantom head. Real-time aerosol measurements (particle size range 0.0062-9.6 μm) were acquired from six locations within a typical dental treatment room (35 m3).

Results: The majority (>99%) of AGP particles were <0.3 μm diameter and remained at elevated levels around the dental team during the AGPs. With no active aerosol-management interventions, AGP particles were estimated to remain above the baseline range for up to 30 minutes from the end of the sequence of procedures.

Conclusions: The results emphasise the importance of personal protection equipment, particularly respiratory protection. Use of HVS(IO), either alone or in combination with the ACS, reduced particle concentrations to baseline levels on completion of AGPs. These data indicate potential to eliminate fallow time. The study was performed using a phantom head so confirmatory studies with patients are required.

Reference

https://www.nature.com/articles/s41415-020-2504-8

SPOTLIGHT

Publication Date: Jan 07, 2021

Altered cholesterol and lipid synthesis mediates hyperinflammation in COVID-19

Recent data have revealed that fructose-rich diet triggers inflammation and lipid synthesis. Furthermore, lipid metabolism, cholesterol synthesis and sterol regulatory element binding protein-2 (SREBP-2) activation correlates with coronavirus disease 2019 (COVID-19)-induced cytokine storm. High fructose consumption result in SREBPs activation, altered cholesterol and lipid synthesis and may establish an innate immune memory in the cells, leading to severe COVID-19 in patients with obesity. For more details, read the link given below.

Reference

https://www.cell.com/trends/endocrinology-metabolism/fulltext/S1043-2760(21)00001-1

PERSPECTIVE

Publication Date: Jan 13, 2021

Immune determinants of COVID-19 disease presentation and severity

COVID-19, caused by SARS-CoV-2 infection, is mild to moderate in the majority of previously healthy individuals, but can cause life-threatening disease or persistent debilitating symptoms in some cases. The most important determinant of disease severity is age, with individuals over 65 years having the greatest risk of requiring intensive care, and men are more susceptible than women. In contrast to other respiratory viral infections, young children seem to be less severely affected. It is now clear that mild to severe acute infection is not the only outcome of COVID-19, and long-lasting symptoms are also possible. In contrast to severe acute COVID-19, such 'long COVID' is seemingly more likely in women than in men. Also, postinfectious hyperinflammatory disease has been described as an additional outcome after SARS-CoV-2 infection. Here, current understanding of the immunological determinants of COVID-19 disease presentation and severity was discussed, and relate this to known immune-system differences between young and old people and between men and women, and other factors associated with different disease presentations and severity. For more details, read the link given below.

Reference

https://www.nature.com/articles/s41591-020-01202-8

COVID-19, obesity, and structural racism: Understanding the past and identifying solutions for the future

Longstanding systemic inequalities – fueling unequal access to critical resources such as healthcare, housing, education, and employment opportunities – are largely responsible for the significant race disparities in obesity and COVID-19. Because of this legacy, public health emergencies like the COVID-19 pandemic disproportionately impact communities of color, exacerbated by high rates of pre-existing chronic diseases like obesity. Learning from this history is instructive for understanding our present situation and for crafting effective solutions which promote health equity. Critical action

is needed now to meaningfully address the disproportionate impact of these major public health problems on Black and Brown populations. For more details, read the link given below.

Reference

https://www.cell.com/cell-metabolism/fulltext/S1550-4131(21)00010-3

Publication Date: Jan 13, 2021

Traitorous COVID antibodies and fast-spreading variant

Antibodies normally attack pathogens, but sometimes rogue antibodies instead besiege bodily components such as immune cells. Now, a new study adds to the growing body of research tying these 'autoantibodies' to poor outcomes in people with COVID-19.

Ana Rodriguez and David Lee at the NYU Grossman School of Medicine in New York City and their colleagues studied autoantibody levels in blood serum collected from 86 people who required hospitalization for COVID-19. The researchers were particularly interested in autoantibodies against the protein annexin A2, which helps to stabilize cell-membrane structure. It also plays a part in ensuring the integrity of tiny blood vessels in the lungs. Blocking annexin A2 leads to lung injury (pictured), a hallmark of COVID-19.

The scientists found that the level of anti-annexin A2 antibodies was, on average, higher in the individuals who eventually died of COVID-19 than in those who survived — a difference that was statistically significant (M. Zuniga et al. Preprint at medRxiv https://doi.org/fqdd; 2021). More research is necessary to establish a clear causal link between the virus SARS-CoV-2 and autoantibodies against annexin A2, which are relatively rare. The findings have not yet been peer reviewed. For more details, read the link given below.

Reference

https://www.nature.com/articles/d41586-021-00017-y

Publication Date: Jan 11, 2021

How can countries stretch COVID vaccine supplies? Scientists are divided over dosing strategies

Amid skyrocketing coronavirus infections, some countries are attempting to stretch limited supplies of COVID-19 vaccines by reducing doses or changing vaccination schedules from those shown to be effective in clinical trials. But data are scarce on the impact of such measures, and scientists are split over whether they are worth the risks.

On 30 December, the United Kingdom announced that it would allow doses of two coronavirus vaccines to be administered as many as 12 weeks apart, even though, in clinical trials, the two doses of the vaccine made by Pfizer of New York City and BioNTech of Mainz, Germany, were given to participants about three weeks apart. By delaying the second jab, the government hopes to free up doses to inoculate more people with their first shot during the current surge. Similar changes have been discussed in other countries, including the United States. Current US policy is to hold doses of the vaccine in reserve to guarantee recipients a second shot, but the transition team of president-elect Joseph Biden is reportedly considering an end to that. And Moncef Slaoui, head of the country's Operation Warp Speed coronavirus-vaccine effort, has suggested that one vaccine — developed by Moderna of Cambridge, Massachusetts, and the US National Institute of Allergy and Infectious Diseases in Bethesda, Maryland — could be given at half the dose used in its largest clinical trial. "These are all reasonable questions to consider and evaluate in clinical trials," said Stephen Hahn, chief of the US Food and Drug Administration (FDA), in a statement released on 4 January. "However, at this time, suggesting changes to the FDA-authorized dosing or schedules of these vaccines is premature and not rooted solidly in the available evidence." On 8 January, the World Health Organization (WHO) recommended a wait of no more than six weeks between the first and second doses of the Pfizer vaccine. "That doesn't mean it's a criticism of what the UK or any other country is doing," says Alejandro Cravioto, chair of the WHO's Strategic Advisory Group of Experts on Immunization. "It is just based on the evidence that we have. For more details, read the link given below.

Reference

https://www.nature.com/articles/d41586-021-00001-6

COMMENT

Publication Date: Jan 12, 2021

Improving family access to dying patients during the COVID-19 pandemic

In response to the COVID-19 pandemic, most health-care organisations have implemented policies to restrict visitor access. Although there are exceptions to some of these policies, including limited visiting for patients nearing the end of life, they still have profound effects on the dying and their family members. We are still in the midst of the pandemic, but there are compelling reasons to expand access of family members to their loved ones as they near the end of life, despite the risk of infection.

Hospital visitor policies represent an attempt to balance two competing priorities. Restrictions reduce the chance of harm from infection, but increase the chance of harm from isolation or separation. Exemptions can reduce isolation and allow for a more compassionate response to patients nearing the end of life, but they potentially increase the risk of COVID-19 transmission. For more details, read the link given below.

Reference

https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00025-4/fulltext

COVID-19 and systemic sclerosis: Clinicopathological implications from Italian nationwide survey study

The ongoing COVID-19 pandemic caused by the novel β-coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), poses a serious challenge for the management of patients with different pre-existing comorbidities, including rheumatic autoimmune systemic diseases. These diseases affect a non-negligible proportion of individuals worldwide and are characterised by profound immune system alterations and increased susceptibility to infections, frequently aggravated by immune-modulating therapies.

Among autoimmune systemic diseases, patients with connective tissue diseases or systemic vasculitis showed a higher prevalence of symptomatic SARS-CoV-2 infection (ie, COVID-19) than did patients with chronic arthritis. Systemic sclerosis represents

one of the most severe connective tissue diseases with multi-organ involvement due to concomitancy of fibrosing and microvascular alterations. However, the literature on the impact of COVID-19 in patients with systemic sclerosis is limited to anecdotal reports or single-centre survey studies focusing on a miscellanea of rheumatic autoimmune disorders. For more details, read the link given below.

Reference

https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(21)00007-2/fulltext

Publication Date: Jan 11, 2021

Implications of COVID-19 sequelae for health-care personnel

The COVID-19 pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was initially described as causing a severe acute respiratory syndrome. Clinical studies have since shown that COVID-19 is a systemic illness with the potential for multiorgan complications. As the pandemic unfortunately continues, COVID-19 has the potential for a broader and more insidious effect, including the loss of skilled health-care personnel to post-COVID-19 disabilities.

Persistent and diverse postviral symptoms have been described in survivors of COVID-19, including those with a mild initial disease course. The development of neuropsychiatric disturbances following a viral infection is well known to health-care providers (i.e., postviral syndrome or in this case, so-called long COVID). Postviral neurological sequelae have been described following infections such as with influenza virus, West Nile virus, Ebola virus, and Zika virus, and after herpes virus reactivation. Despite the known relationship between infections and postviral syndromes, the pathophysiology of postinfectious neurological complications and risk factors are unclear. Overwhelming fatigue with altered sleep, postexertional neurological exhaustion, multidomain cognitive dysfunction, persistent headaches, demyelinating syndromes, peripheral neuropathy, and autonomic instability are prominent features in postviral syndromes; similar concerns present among people with persistent COVID-19 symptoms. Currently, no curative treatments are available for postviral syndromes. Therapy is directed at symptom alleviation and coping strategies. Additionally, the economic effect of postviral syndromes can be substantial, including loss of productivity

and employment, and increased need for disability benefits and financial support. For more details, read the link given below.

Reference

https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30575-0/fulltext

Improving clinical management of COVID-19: The role of prediction models

A year after the identification of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and its related disease, COVID-19, in the Chinese province of Hubei, one of the most difficult-to-manage modern health-care crises has unfolded worldwide. WHO declared COVID-19 a pandemic in March, 2020, and the epidemiological severity has since been shown by the high incidence of infections, critical cases, and deaths from the disease and, indirectly, by tragic socioeconomic disruption.

The long wait to confirm the epidemiological effectiveness of immunisation against COVID-19, based on a confident estimation of vaccine efficacy and safety, should be accompanied by the retention of preventive interventions (i.e., physical distancing, hand hygiene, face masks, ventilation), which have been the only effective measures available until now. For more details, read the link given below.

Reference

https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00006-0/fulltext

SARS-CoV-2 vaccination in patients with liver disease: Responding to the next big question

Since the onset of the COVID-19 pandemic, SARS-CoV-2 vaccine development has progressed at an unprecedented rate, with recent phase 3 trial data offering the tantalising prospect of achieving herd immunity. Until now, researchers have focused on the contribution of specific liver disease phenotypes, including transplantation and immunosuppression, to COVID-19 susceptibility and outcome. However, the hepatology community must now urgently turn its attention to characterising SARS-CoV-2 vaccine responses in these vulnerable patient groups.

The Pfizer/BioNTech BNT162b2 mRNA, Moderna mRNA-1273, and the AstraZeneca/University of Oxford ChAdOx1-nCoV-19 chimpanzee adenovirus (ChAd)

vector vaccines have each reported excellent safety profiles, marked efficacy in preventing symptomatic COVID-19 (62–95%), and have all gained rapid regulatory approval. Currently, it remains unclear why a significant minority of those vaccinated appear susceptible to SARS-CoV-2, although both host factors (eg, underlying chronic diseases or genetic susceptibility) and viral factors (eg, high viral load exposure, specific viral variants) are likely to have a contributory role. For more details, read the link given below.

Reference

https://www.thelancet.com/journals/langas/article/PIIS2468-1253(21)00008-X/fulltext

Publication Date: Jan 13, 2021

Zooanthroponotic potential of SARS-CoV-2 and implications of re-introduction into human population

The emergence of alternate variants of SARS-CoV-2 due to ongoing adaptations in humans and following human-to-animal transmission has raised concern over the efficacy of vaccines against new variants. It was described human-to-animal transmission (zooanthroponosis) of SARS-CoV-2, and its implications for faunal virus persistence and vaccine-mediated immunity. For more details, read the link given below.

Reference

https://www.cell.com/cell-host-microbe/fulltext/S1931-3128(21)00034-2

CORRESPONDANCE

Publication Date: Jan 07, 2021

Thromboses and COVID-19: Reducing inflammation in addition to thromboprophylaxis

The COVID-19 pandemic is an unprecedented global health-care emergency, with high mortality in patients who develop COVID-19 pneumonia. These patients have a prothrombotic state with both venous and arterial thrombi occurring despite thromboprophylaxis. Prothrombotic mechanisms are multifactorial, with immune activation leading to an acute phase response, resulting in elevated plasma coagulation factors (particularly fibrinogen). Other features include platelet hyperreactivity, the effects of hypoxia, formation of neutrophil extracellular traps, and complement activation. Although very high circulating D-dimer concentrations are observed in patients with COVID-19, there is little evidence of disseminated intravascular coagulation, as thrombocytopenia and hypofibrinogenaemia are not present and screening clotting times are not prolonged. Many mechanisms driving thromboses in patients with COVID-19 have been suggested, including inflammatory activation of endothelial cells. It was believed that the pathogenesis of thrombosis in patients with COVID-19 pneumonia shares similarities with that in patients with Behçet's syndrome.

Behçet's syndrome is a multisystem vasculitis, most commonly characterised by recurrent orogenital ulcers and uveitis. Vascular involvement affects 10–30% of people with Behçet's syndrome, causing mainly superficial or deep venous thrombosis. Vascular wall inflammation, rather than a hypercoagulable state, is the main cause of thromboses in patients with Behçet's syndrome. Hence, treatment guidelines endorse immunosuppression (including steroids and tumour necrosis factor blockade) and discourage the use of anticoagulation, mainly due to the perceived risk of bleeding from covert pulmonary arterial aneurysms, which is not present in patients with COVID-19. Although pulmonary emboli are described in patients with Behçet's syndrome and patients with COVID-19, this term could be misleading, as segmental and subsegmental changes seen on CT pulmonary angiograms might not be caused by emboli but by immunothrombosis or in-situ thrombosis due to local inflammation. There are

histological similarities in the two conditions. In patients with Behçet's syndrome, thrombi are tightly adherent to the vessel wall, and some thrombus casts in patients with COVID-19 have been shown to conform to the pulmonary artery vasculature (suggesting in-situ anatomical origin) and to occur without an overt distal embolic source, such as deep venous thrombosis. Therefore, pulmonary inflammation is likely to drive thrombosis in both patients with Behçet's syndrome and patients with COVID-19. For more details, read the link given below.

Reference

https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(21)00003-5/fulltext

VIEWPOINT

Publication Date: Jan 07, 2021

COVID-19 vasculitis and novel vasculitis mimics

COVID-19 has been occasionally linked to histologically confirmed cutaneous vasculitis and a Kawasaki-like vasculitis, with these entities generally having minimal or no lung involvement and a good prognosis. Unlike these vasculitis types, patients with severe COVID-19 pneumonia can develop cutaneous vasculitis-like lesions and systemic arterial and venous thromboemboli, including cryptogenic strokes and other vasculopathy features. Proposed underlying mechanisms for these severe manifestations have encompassed immune dysregulation, including an anti-phospholipid syndrome-like state, complement activation, viral dissemination with direct systemic endothelial infection, viral RNAaemia with immunothrombosis, clotting pathway activation mediated by hypoxaemia, and immobility. In this Viewpoint, we highlight how imaging and post-mortem findings from patients with COVID-19 indicate a novel thrombosis in the pulmonary venous territory distal to the alveolar capillary bed, a territory that normally acts as a clot filtration system, which might represent an unappreciated nidus for systemic microembolism. Additionally, we suggest that this mechanism represents a novel vasculitis mimic related to COVID-19 that might lead to cryptogenic strokes across multivessel territories, acute kidney injury with haematuria, a skin vasculitis mimic, intestinal ischaemia, and other organ ischaemic manifestations. This finding is supported by pathological reports of extensive pulmonary venular thrombosis and peripheral organ thrombosis with pauci-immune cellular infiltrates. Therefore, severe COVID-19 pneumonia with extensive pulmonary intravascular coagulopathy might help to explain the numerous systemic complications of COVID-19, in which the demonstration of direct organ infection has not adequately explained the pathology. For more details, read the link given below.

Reference

https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(20)30420-3/fulltext

REPORT

Publication Date: Jan 12, 2021

Mosaic nanoparticles elicit cross-reactive immune responses to zoonotic coronaviruses in mice

Protection against SARS-CoV-2 and SARS-related emergent zoonotic coronaviruses is urgently needed. We made homotypic nanoparticles displaying the receptor-binding domain (RBD) of SARS-CoV-2 or co-displaying SARS-CoV-2 RBD along with RBDs from animal betacoronaviruses that represent threats to humans (mosaic nanoparticles; 4-8 distinct RBDs). Mice immunized with RBD-nanoparticles, but not soluble antigen, elicited cross-reactive binding and neutralization responses. Mosaic-RBD-nanoparticles elicited antibodies with superior cross-reactive recognition of heterologous RBDs compared to sera from immunizations with homotypic SARS-CoV-2–RBD-nanoparticles or COVID-19 convalescent human plasmas. Moreover, sera from mosaic-RBD–immunized mice neutralized heterologous pseudotyped coronaviruses equivalently or better after priming than sera from homotypic SARS-CoV-2–RBD-nanoparticle immunizations, demonstrating no immunogenicity loss against particular RBDs resulting from co-display. A single immunization with mosaic-RBD-nanoparticles provides a potential strategy to simultaneously protect against SARS-CoV-2 and emerging zoonotic coronaviruses. For more details, read the link given below.

Reference

https://science.sciencemag.org/content/early/2021/01/11/science.abf6840

Immunological characteristics govern the transition of COVID-19 to endemicity

It was currently faced with the question of how the CoV-2 severity may change in the years ahead. The analysis of immunological and epidemiological data on endemic human coronaviruses (HCoVs) shows that infection-blocking immunity wanes rapidly, but disease-reducing immunity is long-lived. The model, incorporating these components of immunity, recapitulates both the current severity of CoV-2 and the benign nature of HCoVs, suggesting that once the endemic phase is reached and primary exposure is in childhood, CoV-2 may be no more virulent than the common

cold. We predict a different outcome for an emergent coronavirus that causes severe disease in children. These results reinforce the importance of behavioral containment during pandemic vaccine rollout, while prompting us to evaluate scenarios for continuing vaccination in the endemic phase. For more details, read the link given below.

Reference

https://science.sciencemag.org/content/early/2021/01/11/science.abe6522

Publication Date: Jan 08, 2021

Establishment and lineage dynamics of the SARS-CoV-2 epidemic in the UK

The UK's COVID-19 epidemic during early 2020 was one of world's largest and unusually well represented by virus genomic sampling. Here, it was revealed that the fine-scale genetic lineage structure of this epidemic through analysis of 50,887 SARS-CoV-2 genomes, including 26,181 from the UK sampled throughout the country's first wave of infection. Using large-scale phylogenetic analyses, combined with epidemiological and travel data, we quantify the size, spatio-temporal origins and persistence of genetically-distinct UK transmission lineages. Rapid fluctuations in virus importation rates resulted in >1000 lineages; those introduced prior to national lockdown tended to be larger and more dispersed. Lineage importation and regional lineage diversity declined after lockdown, while lineage elimination was size-dependent. The implications of our genetic perspective on transmission dynamics was discussed for COVID-19 epidemiology and control. For more details, read the link given below.

Reference

https://science.sciencemag.org/content/early/2021/01/07/science.abf2946