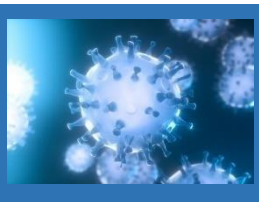

RESEARCH PUBLICATIONS

Publication Date: Feb 24, 2021

Comparison of the clinical characteristics and mortality of adults infected with human coronaviruses 229E and OC43

Abstract

The purpose of the study was to compare clinical characteristics and mortality among adults infected with human coronaviruses (HCoV) 229E and OC43. A retrospective cohort study was conducted of adults (≥ 18 years) admitted to the ward of a university teaching hospital for suspected viral infection from October 2012 to December 2017. Multiplex real-time polymerase chain reaction (PCR) was used to test for respiratory viruses. Multivariate logistic regression was used to compare mortality among patients with HCoV 229E and HCoV OC43 infections. The main outcome was 30-day all-cause mortality. Of 8071 patients tested, 1689 were found to have a respiratory virus infection. Of these patients, 133 had HCoV infection, including 12 mixed infections, 44 HCoV 229E infections, and 77 HCoV OC43 infections. HCoV 229E infections peaked in January and February, while HCoV OC43 infections occurred throughout the year. The 30-day all-cause mortality was 25.0% among patients with HCoV 229E infection, and 9.1% among patients with HCoV OC43 infection (adjusted odds ratio: 3.58, 95% confidence interval: 1.19–10.75). Infections with HCoVs 229E and OC43 appear to have different seasonal patterns, and HCoV 229E might be more virulent than HCoV OC43.

Reference

https://www.nature.com/articles/s41598-021-83987-3

Achieving herd immunity against COVID-19 at the country level by the exit strategy of a phased lift of control

Abstract

The COVID-19 pandemic has affected the entire world causing substantial numbers of cases and deaths in most countries. Many have implemented nationwide stringent control to avoid overburdening the health care system. This has paralyzed economic and social activities and may continue to do so until the large-scale availability of a vaccine. An alternative exit strategy was propsed to develop herd immunity in a predictable and controllable way: a phased lift of control. This means that successive parts of the country (e.g. provinces) stop stringent control, and COVID-19-related IC admissions are distributed over the country as a whole. Importantly, vulnerable individuals need to be shielded until herd immunity has developed in their area. We explore the characteristics and duration of this strategy using a novel individual-based model for geographically stratified transmission of COVID-19 in a country. The model predicts that individuals will have to experience stringent control for about 14 months on average, but this duration may be almost halved by further developments (more IC beds, better treatments). Clearly, implementation of this strategy would have a profound impact on individuals and society, and should therefore be considered carefully by various other disciplines (*e.g.* health systems, ethics, economics) before actual implementation.

Reference

https://www.nature.com/articles/s41598-021-83492-7

COVID-19 mental health impact and responses in low-income and middle-income countries: Reimagining global mental health

Abstract

Most of the global population live in low-income and middle-income countries (LMICs), which have historically received a small fraction of global resources for mental health. The COVID-19 pandemic has spread rapidly in many of these countries. This Review examines the mental health implications of the COVID-19 pandemic in LMICs in four parts. First, we review the emerging literature on the impact of the pandemic on mental

health, which shows high rates of psychological distress and early warning signs of an increase in mental health disorders. Second, we assess the responses in different countries, noting the swift and diverse responses to address mental health in some countries, particularly through the development of national COVID-19 response plans for mental health services, implementation of WHO guidance, and deployment of digital platforms, signifying a welcome recognition of the salience of mental health. Third, we consider the opportunity that the pandemic presents to reimagine global mental health, especially through shifting the balance of power from high-income countries to LMICs and from narrow biomedical approaches to community-oriented psychosocial perspectives, in setting priorities for interventions and research. Finally, a vision was presented for the concept of building back better the mental health systems in LMICs with a focus on key strategies; notably, fully integrating mental health in plans for universal health coverage, enhancing access to psychosocial interventions through task sharing, leveraging digital technologies for various mental health tasks, eliminating coercion in mental health care, and addressing the needs of neglected populations, such as children and people with substance use disorders. The recommendations are relevant for the mental health of populations and functioning of health systems in not only LMICs but also high-income countries impacted by the COVID-19 pandemic, with wide disparities in quality of and access to mental health care.

Reference

https://www.thelancet.com/journals/lanpsy/article/PIIS2215-0366(21)00025-0/fulltext

In- and out-of-hospital mortality for myocardial infarction during the first wave of the COVID-19 pandemic in Emilia-Romagna, Italy: A population-based observational study

Abstract

Background: The COVID-19 pandemic has put several healthcare systems under severe pressure. The present analysis investigates how the first wave of the COVID-19 pandemic affected the myocardial infarction (MI) network of Emilia-Romagna (Italy).

Methods: Based on Emilia-Romagna mortality registry and administrative data from all the hospitals from January 2017 to June 2020, we analysed: i) temporal trend in MI

hospital admissions; ii) characteristics, management, and 30-day mortality of MI patients; iii) out-of-hospital mortality for cardiac cause.

Findings: Admissions for MI declined on February 22, 2020 (IRR -19.5%, 95%CI from -8.4% to -29.3%, p = 0.001), and further on March 5, 2020 (IRR -21.6%, 95%CI from -9.0% to -32.5%, p = 0.001). The return to pre-COVID-19 MI-related admission levels was observed from May 13, 2020 (IRR 34.3%, 95%CI 20.0%-50.2%, p<0.001). As compared to those before the pandemic, MI patients admitted during and after the first wave were younger and with fewer risk factors. The 30-day mortality remained in line with that expected based on previous years (ratio observed/expected was 0.96, 95%CI 0.84–1.08). MI patients positive for SARS-CoV-2 were few (1.5%) but showed poor prognosis (around 5-fold increase in 30-day mortality). In 2020, the number of out-of-hospital cardiac deaths was significantly higher (ratio observed/expected 1.17, 95%CI 1.08–1.27). The peak was reached in April.

Interpretation: In Emilia-Romagna, MI hospitalizations significantly decreased during the first wave of the COVID-19 pandemic. Management and outcomes of hospitalized MI patients remained unchanged, except for those with SARS-CoV-2 infection. A concomitant increase in the out-of-hospital cardiac mortality was observed.

Reference

https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762(21)00032-6/fulltext

Limited window for donation of convalescent plasma with high live-virus neutralizing antibody titers for COVID-19 immunotherapy

Abstract

Millions of individuals who have recovered from SARS-CoV-2 infection may be eligible to participate in convalescent plasma donor programs, yet the optimal window for donating high neutralizing titer convalescent plasma for COVID-19 immunotherapy remains unknown. Here we studied the response trajectories of antibodies directed to the SARS-CoV-2 surface spike glycoprotein and in vitro SARS-CoV-2 live virus neutralizing titers (VN) in 175 convalescent donors longitudinally sampled for up to 142 days post onset of symptoms (DPO). Robust IgM, IgG, and viral neutralization responses were observed to SARS-CoV-2 that persist, in the aggregate, for at least 100

DPO. However, there is a notable decline in VN titers ≥160 for convalescent plasma therapy, starting 60 DPO. The results also show that individuals 30 years of age or younger have significantly lower VN, IgG and IgM antibody titers than those in the older age groups; and individuals with greater disease severity also have significantly higher IgM and IgG antibody titers. Taken together, these findings define the optimal window for donating convalescent plasma useful for immunotherapy of COVID-19 patients and reveal important predictors of an ideal plasma donor.

Reference

https://www.nature.com/articles/s42003-021-01813-y

Identification of candidate repurposable drugs to combat COVID-19 using a signature-based approach

Abstract

The COVID-19 pandemic caused by the novel SARS-CoV-2 is more contagious than other coronaviruses and has higher rates of mortality than influenza. Identification of effective therapeutics is a crucial tool to treat those infected with SARS-CoV-2 and limit the spread of this novel disease globally. We deployed a bioinformatics workflow to identify candidate drugs for the treatment of COVID-19. Using an “omics” repository, the Library of Integrated Network-Based Cellular Signatures (LINCS), transcriptomic signatures of putative COVID-19 drugs were simultaneously probed and publicly available SARS-CoV-2 infected cell lines to identify novel therapeutics. A shortlist of 20 candidate drugs were identified: 8 are already under trial for the treatment of COVID-19, the remaining 12 have antiviral properties and 6 have antiviral efficacy against coronaviruses specifically*, in vitro*. All candidate drugs are either FDA approved or are under investigation. The candidate drug findings are discordant with (i.e., reverse) SARS-CoV-2 transcriptome signatures generated in vitro, and a subset are also identified in transcriptome signatures generated from COVID-19 patient samples, like the MEK inhibitor selumetinib. Overall, the findings provide additional support for drugs that are already being explored as therapeutic agents for the treatment of COVID-19 and identify promising novel targets that are worthy of further investigation.

Reference

https://www.nature.com/articles/s41598-021-84044-9

Equivalent SARS-CoV-2 viral loads by PCR between nasopharyngeal swab and saliva in symptomatic patients

Abstract

Emerging evidences have shown the utility of saliva for the detection of SARS-CoV-2 by PCR as alternative to nasopharyngeal swab (NPS). However, conflicting results have been reported regarding viral loads between NPS and saliva. We conducted a study to compare the viral loads between NPS and saliva in 42 COVID-19 patients. Viral loads were estimated by the cycle threshold (Ct) values. SARS-CoV-2 was detected in 34 (81%) using NPS with median Ct value of 27.4, and 38 (90%) using saliva with median Ct value of 28.9 (P = 0.79). Kendall's W was 0.82, showing a high degree of agreement, indicating equivalent viral loads in NPS and saliva. After symptom onset, the Ct values of both NPS and saliva continued to increase over time, with no substantial difference. Self-collected saliva has a detection sensitivity comparable to that of NPS and is a useful diagnostic tool with mitigating uncomfortable process and the risk of aerosol transmission to healthcare workers.

Reference

https://www.nature.com/articles/s41598-021-84059-2

SARS-CoV-2 vaccine testing and trials in the pediatric population: Biologic, ethical, research, and implementation challenges

Abstract

As the nation implements SARS-CoV-2 vaccination in adults at an unprecedented scale, it is now essential to focus on the prospect of SARS-CoV-2 vaccinations in pediatric populations. To date, no children younger than 12 years have been enrolled in clinical trials. Key challenges and knowledge gaps that must be addressed include (1) rationale for vaccines in children, (2) possible effects of immune maturation during childhood, (3) ethical concerns, (4) unique needs of children with developmental disorders and chronic conditions, (5) health inequities, and (6) vaccine hesitancy. Because COVID-19 is minimally symptomatic in the vast majority of children, a higher

acceptable risk threshold is required when evaluating pediatric clinical trials. Profound differences in innate and adaptive immunity during childhood and adolescence are known to affect vaccine responsiveness for a variety of childhood diseases. COVID-19 and the accompanying social disruption, such as the school shutdowns, has been disproportionately damaging to minority and low-income children. In this commentary, we briefly address each of these key issues, specify research gaps, and suggest a broader learning health system approach to accelerate testing and clinical trial development for an ethical and effective strategy to implement a pediatric SARS-CoV-2 vaccine as rapidly and safely as possible.

Reference

https://www.nature.com/articles/s41390-021-01402-z

Comparison of rhesus and cynomolgus macaques as an infection model for COVID-19

Abstract

A novel coronavirus, SARS-CoV-2, has been identified as the causative agent of the current COVID-19 pandemic. Animal models, and in particular non-human primates, are essential to understand the pathogenesis of emerging diseases and to assess the safety and efficacy of novel vaccines and therapeutics. Here, it was shown that SARS-CoV-2 replicates in the upper and lower respiratory tract and causes pulmonary lesions in both rhesus and cynomolgus macaques. Immune responses against SARS-CoV-2 are also similar in both species and equivalent to those reported in milder infections and convalescent human patients. This finding is reiterated by our transcriptional analysis of respiratory samples revealing the global response to infection. A new method was described for lung histopathology scoring that will provide a metric to enable clearer decision making for this key endpoint. In contrast to prior publications, in which rhesus are accepted to be the preferred study species, we provide convincing evidence that both macaque species authentically represent mild to moderate forms of COVID-19 observed in the majority of the human population and both species should be used to evaluate the safety and efficacy of interventions against SARS-CoV-2. Importantly, accessing cynomolgus macaques will greatly alleviate the pressures on current rhesus stocks.

Reference

https://www.nature.com/articles/s41467-021-21389-9

Association of coagulation dysfunction with cardiac injury among hospitalized patients with COVID-19

Abstract

Cardiac injury is a common complication of the coronavirus disease 2019 (COVID-19), and is associated with adverse clinical outcomes. In this study, it was aimed to reveal the association of cardiac injury with coagulation dysfunction. 181 Consecutive patients were enrolled who were hospitalized with COVID-19, and studied the clinical characteristics and outcome of these patients. Cardiac biomarkers high-sensitivity troponin I (hs-cTnI), myohemoglobin and creatine kinase-myocardial band (CK-MB) were assessed in all patients. The clinical outcomes were defined as hospital discharge or death. The median age of the study cohort was 55 (IQR, 46–65) years, and 102 (56.4%) were males. Forty-two of the 181 patients (23.2%) had cardiac injury. Old age, high leukocyte count, and high levels of aspartate transaminase (AST), D-dimer and serum ferritin were significantly associated with cardiac injury. Multivariate regression analysis revealed old age and elevated D-dimer levels as being strong risk predictors of in-hospital mortality. Interleukin 6 (IL6) levels were comparable in patients with or without cardiac injury. Serial observations of coagulation parameters demonstrated highly synchronous alterations of D-dimer along with progression to cardiac injury. Cardiac injury is a common complication of COVID-19 and is an independent risk factor for in-hospital mortality. Old age, high leukocyte count, and high levels of AST, D-dimer and serum ferritin are significantly associated with cardiac injury, whereas IL6 are not. Therefore, the pathogenesis of cardiac injury in COVID-19 may be primarily due to coagulation dysfunction along with microvascular injury.

Reference

https://www.nature.com/articles/s41598-021-83822-9

The impact of oral health status on COVID-19 severity, recovery period and C-reactive protein values

Abstract

Objectives: The oral cavity is a potential reservoir for respiratory pathogens which can predispose patients to bacterial super-infection. Several trials have correlated poor oral hygiene with hyper-inflammation. Similarly, COVID-19 severity has been linked to hyper-inflammatory responses. Hence, in this study, we assumed that increased COVID-19 severity may be linked to poor oral health status. This was achieved through assessing oral health status, severity of COVID-19 symptoms, C-reactive protein (CRP) levels and duration of recovery.

Methods: Cross-sectional study based on a questionnaire; 308 Egyptian patients with confirmed positive polymerase chain reaction (PCR) tests were included in the study after exclusion criteria. The questionnaire was designed with two sections: the first section for oral health evaluation and the second section for COVID-19 severity evaluation. Assessment of the effect of oral health on COVID-19 severity was performed using an oral health score. The effect of oral health on CRP and recovery period were evaluated as secondary endpoints. Data of CRP levels and COVID-19 PCR tests were collected via the questionnaire and confirmed by reviewing medical records.

Results: The correlation between oral health and COVID-19 severity showed a significant inverse correlation ($p < 0.001$, $r = -0.512$). Moreover, the correlation between oral health with recovery period and CRP values also revealed a significant inverse correlation ($p < 0.001$, -0.449 and $p < 0.001$, -0.190, respectively), showing that poor oral health was correlated to increased values of CRP and delayed recovery period.

Conclusions: Our study provided some evidence that oral health could have a potential impact on the severity of COVID-19. However, the correlation is limited by the study design. A more substantial research project is required to address this relation.

Reference

https://www.nature.com/articles/s41415-021-2656-1

Therapeutic activity of an inhaled potent SARS-CoV-2 neutralizing human monoclonal antibody in hamsters

Abstract

SARS-CoV-2 infection results in viral burden in the respiratory tract, enabling transmission and leading to substantial lung pathology. The 1212C2 fully human monoclonal antibody was derived from an IgM memory B cell of a COVID-19 patient, has high affinity for the Spike protein Receptor Binding Domain, neutralizes SARS-CoV-2 and exhibits in vivo prophylactic and therapeutic activity in hamsters when delivered intraperitoneally, reducing upper and lower respiratory viral burden and lung pathology. Inhalation of nebulized 1212C2 at levels as low as 0.6mg/kg, corresponding to 0.03mg/kg of lung deposited dose, reduced viral burden below the detection limit, and mitigated lung pathology. The therapeutic efficacy of an exceedingly low-dose of inhaled 1212C2 supports the rationale for local lung delivery for dose-sparing benefits as compared to the conventional parenteral route of administration. These results suggest clinical development of 1212C2 formulated and delivered via inhalation for the treatment of SARS-CoV-2 infection should be considered.

Reference

https://www.cell.com/cell-reports-medicine/fulltext/S2666-3791(21)00034-3

Robust SARS-CoV-2 infection in nasal turbinates after treatment with systemic neutralizing antibodies

Abstract

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is characterized by a burst in the upper respiratory portal for high transmissibility. To determine human neutralizing antibodies (HuNAbs) for entry protection, three potent HuNAbs (IC_{50} range, 0.0007-0.35 μg/ml) were tested against live SARS-CoV-2 infection in the golden Syrian hamster model. These HuNAbs inhibit SARS-CoV-2 infection by competing with human angiotensin converting enzyme-2 for binding to the viral receptor binding domain (RBD). Prophylactic intraperitoneal or intranasal injection of individual HuNAb or DNA vaccination significantly reduces infection in the lungs but not in the nasal turbinates of hamsters intranasally challenged with SARS-CoV-2. Although postchallenge HuNAb

therapy suppresses viral loads and lung damage, robust infection is observed in nasal turbinates treated within 1-3 days. The findings demonstrate that systemic HuNAb suppresses SARS-CoV-2 replication and injury in lungs; however, robust viral infection in nasal turbinate may outcompete the antibody with significant implications to subprotection, reinfection and vaccine.

Reference

https://www.cell.com/cell-host-microbe/fulltext/S1931-3128(21)00098-6

Publication Date: Feb 23, 2021

Evidence of escape of SARS-CoV-2 variant B.1.351 from natural and vaccine induced sera

Abstract

The race to produce vaccines against SARS-CoV-2 began when the first sequence was published, and this forms the basis for vaccines currently deployed globally. Independent lineages of SARS-CoV-2 have recently been reported: UK–B.1.1.7, South Africa–B.1.351 and Brazil–P.1. These variants have multiple changes in the immunodominant spike protein which facilitates viral cell entry via the Angiotensin converting enzyme-2 (ACE2) receptor. Mutations in the receptor recognition site on the spike are of great concern for their potential for immune escape. Here we describe a structure-function analysis of B.1.351 using a large cohort of convalescent and vaccinee serum samples. The receptor binding domain mutations provide tighter ACE2 binding and widespread escape from monoclonal antibody neutralization largely driven by E484K although K417N and N501Y act together against some important antibody classes. In a number of cases it would appear that convalescent and some vaccine serum offers limited protection against this variant.

Reference

https://www.cell.com/cell/fulltext/S0092-8674(21)00226-9

Extremely potent human monoclonal antibodies from COVID-19 convalescent patients

Abstract

Human monoclonal antibodies are safe, preventive and therapeutic tools, that can be rapidly developed to help restore the massive health and economic disruption caused by the coronavirus disease 2019 (COVID-19) pandemic. By single cell sorting 4,277 SARS-CoV-2 spike protein specific memory B cells from 14 COVID-19 survivors, 453 neutralizing antibodies were identified. The most potent neutralizing antibodies recognized the spike protein receptor binding domain, followed in potency by antibodies that recognize the S1 domain, the spike protein trimer and the S2 subunit. Only 1.4% of them neutralized the authentic virus with a potency of 1-10 ng/mL. The most potent monoclonal antibody, engineered to reduce the risk of antibody dependent enhancement and prolong half-life, neutralized the authentic wild type virus and emerging variants containing D614G, E484K and N501Y substitutions. Prophylactic and therapeutic efficacy in the hamster model was observed at 0.25 and 4 mg/kg respectively in absence of Fc-functions.

Reference

https://www.cell.com/cell/fulltext/S0092-8674(21)00224-5

A *trans*-complementation system for SARS-CoV-2 recapitulates authentic viral replication without virulence

Abstract

The biosafety level-3 (BSL-3) requirement to culture severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a bottleneck for research. Here a trans-complementation system was reported that produces single-round infectious SARS-CoV-2 that recapitulates authentic viral replication. It was demonstrated that the single-round infectious SARS-CoV-2 can be used at BSL-2 laboratories for high-throughput neutralization and antiviral testing. The trans-complementation system consists of two components: a genomic viral RNA containing ORF3 and envelope gene deletions as well as mutated transcriptional regulator sequences, and a producer cell line expressing the two deleted genes. *Trans*-complementation of the two components generates

virions that can infect naive cells for only one round, but does not produce wild-type SARS-CoV-2. Hamsters and K18-hACE2 transgenic mice inoculated with the complementation-derived virions exhibited no detectable disease, even after intracranial inoculation with the highest possible dose. Thus, the trans-complementation platform can be safely used at BSL-2 laboratories for research and countermeasure development.

Reference

https://www.cell.com/cell/fulltext/S0092-8674(21)00233-6

Use of convalescent serum reduces severity of COVID-19 in nonhuman primates

Abstract

Passive transfer of convalescent plasma or serum is a time-honored strategy for treating infectious diseases. Human convalescent plasma containing antibodies against SARS-CoV-2 is currently being used to treat COVID-19 patients where clinical efficacy trials are ongoing. Here, we assess therapeutic passive transfer in groups of SARS-CoV-2-infected African green monkeys with convalescent sera containing either high or low anti-SARS-CoV-2 neutralizing antibody titers. Differences in viral load and pathology are minimal between monkeys that receive the lower titer convalescent sera and untreated controls. However, lower levels of SARS-CoV-2 in respiratory compartments, reduced severity of virus-associated lung pathology, and reductions in coagulopathy and inflammatory processes are observed in monkeys that receive high titer sera versus untreated controls. The data indicated convalescent plasma therapy in humans may be an effective strategy provided donor sera contain high anti-SARS-CoV-2 neutralizing titers given in early stages of disease.

Reference

https://www.cell.com/cell-reports/fulltext/S2211-1247(21)00151-0

Anxiety and depression due to 2019 SARS-CoV-2 among frontier healthcare workers in Kenya

Abstract

Background: The novel coronavirus disease continues to spread across the globe, causing anxiety and depression among healthcare workers.

Objectives: The current study aimed to determine the levels of anxiety and depression due to the coronavirus pandemic among healthcare workers in Kenya.

Methods: A total sample of 476 respondents participated. The 7-item Generalized Anxiety Disorder Scale (GAD-7) and Patient-Health Questionnaire (PHQ-9), together with a socio-demographic questionnaire, were used. Stratified sampling was used. Data were analysed using the Statistical Package Programme for Social Science Version 23.0.0. Kruskal Wallis test and Mann-Whitney U test were used to establish the difference in levels of anxiety and depression across the socio-economic characteristics. Ordinal logistic regression analysis was used to establish the predictors of levels of anxiety and associations were considered significant at $p<0.05$.

Results: From the total, 35.1% (n=167) had mild anxiety, and 13.4% (n=64) had severe anxiety. Approximately 53.6% (n=255) had mild depression while 9.2% (n=44) had severe depression. The univariate analysis illustrated a statistical difference in anxiety levels in gender ($p>0.002$), years of work experience ($p=0.005$), and the cadre of respondents ($p=0.0028$). Gender was statistically significant with the level of depression ($p=0.045$). About 62.6% (n=298) of healthcare workers had been trained, and only 9% (n=43) were confident in managing COVID-19 cases. A large proportion, 98% (n=458) had concerns about the availability of personal protective equipment.

Conclusion: The study findings indicated that the majority of healthcare workers had mild anxiety. Female healthcare workers were more likely to experience severe anxiety and depression. Also, levels of depression differed across different cadres of respondents.

Reference

https://www.cell.com/heliyon/fulltext/S2405-8440(21)00456-4

Diagnosis, clinical characteristics, and outcomes of COVID-19 patients from a large healthcare system in northern New Jersey

Abstract

New Jersey was an early epicenter for the COVID-19 pandemic in the United States, yet information on hospitalized COVID-19 patients from this area is scarce. This study aimed to provide data on demographics and clinical features of a hospitalized patient population who were confirmed with infection by our in-house (CDI) real-time reverse-transcription polymerase chain reaction (RT-PCR) test. Consecutive patients were included who were admitted to Hackensack Meridian Health system hospitals with laboratory-confirmed diagnoses of COVID-19 at Hackensack University Medical Center by the CDI virus test between March 12, 2020, and April 8, 2020. Clinical data and viral testing results were collected and analyzed for characteristics associated with outcomes, as well as the correlation with viral load. A total of 722 patients were included in the study, with a median age of 63 (interquartile range (IQR), 51–75) and 272 (37.7%) females. Mortality of this case series was 25.8%, with a statistically significant linear increase observed from age 40 to ≥ 80 by 10-year intervals. Viral load, as indicated by the cycle of threshold (Ct) values from the RT-PCR test, was significantly higher in the oldest patient group (≥ 80), and inversely correlated with survival. This is the first report to describe the clinical characteristics and outcomes in a large hospitalized COVID-19 patient series from New Jersey. Findings from this study are valuable to the ongoing response of both nationwide healthcare networks and the medical research community.

Reference

https://www.nature.com/articles/s41598-021-83959-7

Observational study on wearable biosensors and machine learning-based remote monitoring of COVID-19 patients

Abstract

Patients infected with SARS-CoV-2 may deteriorate rapidly and therefore continuous monitoring is necessary. An observational study was conducted involving patients with mild COVID-19 to explore the potentials of wearable biosensors and machine learning-

based analysis of physiology parameters to detect clinical deterioration. Thirty-four patients (median age: 32 years; male: 52.9%) with mild COVID-19 from Queen Mary Hospital were recruited. The mean National Early Warning Score 2 (NEWS2) were 0.59 ± 0.7. 1231 manual measurement of physiology parameters were performed during hospital stay (median 15 days). Physiology parameters obtained from wearable biosensors correlated well with manual measurement including pulse rate ($r = 0.96$, $p < 0.0001$) and oxygen saturation ($r = 0.87$, $p < 0.0001$). A machine learning-derived index reflecting overall health status, Biovitals Index (BI), was generated by autonomous analysis of physiology parameters, symptoms, and other medical data. Daily BI was linearly associated with respiratory tract viral load ($p < 0.0001$) and NEWS2 ($r = 0.75$, $p < 0.001$). BI was superior to NEWS2 in predicting clinical worsening events (sensitivity 94.1% and specificity 88.9%) and prolonged hospitalization (sensitivity 66.7% and specificity 72.7%). Wearable biosensors coupled with machine learning-derived health index allowed automated detection of clinical deterioration.

Reference

https://www.nature.com/articles/s41598-021-82771-7

Biological activity-based modeling identifies antiviral leads against SARS-CoV-2

Abstract

Computational approaches for drug discovery, such as quantitative structure–activity relationship, rely on structural similarities of small molecules to infer biological activity but are often limited to identifying new drug candidates in the chemical spaces close to known ligands. Here a biological activity-based modeling (BABM) approach was reported, in which compound activity profiles established across multiple assays are used as signatures to predict compound activity in other assays or against a new target. This approach was validated by identifying candidate antivirals for Zika and Ebola viruses based on high-throughput screening data. BABM models were then applied to predict 311 compounds with potential activity against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Of the predicted compounds, 32% had antiviral activity in a cell culture live virus assay, the most potent compounds showing a half-maximal inhibitory concentration in the nanomolar range. Most of the confirmed anti-SARS-CoV-2 compounds were found to be viral entry inhibitors and/or autophagy

modulators. The confirmed compounds have the potential to be further developed into anti-SARS-CoV-2 therapies.

Reference

https://www.nature.com/articles/s41587-021-00839-1

Identification and validation of clinical phenotypes with prognostic implications in patients admitted to hospital with COVID-19: A multicentre cohort study

Abstract

Background: The clinical presentation of COVID-19 in patients admitted to hospital is heterogeneous. It was aimed to determine whether clinical phenotypes of patients with COVID-19 can be derived from clinical data, to assess the reproducibility of these phenotypes and correlation with prognosis, and to derive and validate a simplified probabilistic model for phenotype assignment. Phenotype identification was not primarily intended as a predictive tool for mortality.

Methods: In this study, data were used from two cohorts: the COVID-19@Spain cohort, a retrospective cohort including 4035 consecutive adult patients admitted to 127 hospitals in Spain with COVID-19 between Feb 2 and March 17, 2020, and the COVID-19@HULP cohort, including 2226 consecutive adult patients admitted to a teaching hospital in Madrid between Feb 25 and April 19, 2020. The COVID-19@Spain cohort was divided into a derivation cohort, comprising 2667 randomly selected patients, and an internal validation cohort, comprising the remaining 1368 patients. The COVID-19@HULP cohort was used as an external validation cohort. A probabilistic model for phenotype assignment was derived in the derivation cohort using multinomial logistic regression and validated in the internal validation cohort. The model was also applied to the external validation cohort. 30-day mortality and other prognostic variables were assessed in the derived phenotypes and in the phenotypes assigned by the probabilistic model.

Findings: Three distinct phenotypes were derived in the derivation cohort (n=2667)—phenotype A (516 [19%] patients), phenotype B (1955 [73%]) and phenotype C (196 [7%])—and reproduced in the internal validation cohort (n=1368)—phenotype A (233 [17%] patients), phenotype B (1019 [74%]), and phenotype C (116 [8%]). Patients with

phenotype A were younger, were less frequently male, had mild viral symptoms, and had normal inflammatory parameters. Patients with phenotype B included more patients with obesity, lymphocytopenia, and moderately elevated inflammatory parameters. Patients with phenotype C included older patients with more comorbidities and even higher inflammatory parameters than phenotype B. A simplified probabilistic model was developed (validated in the internal validation cohort) for phenotype assignment, including 16 variables. In the derivation cohort, 30-day mortality rates were 2·5% (95% CI 1·4–4·3) for patients with phenotype A, 30·5% (28·5–32·6) for patients with phenotype B, and 60·7% (53·7–67·2) for patients with phenotype C (log-rank test p<0·0001). The predicted phenotypes in the internal validation cohort and external validation cohort showed similar mortality rates to the assigned phenotypes (internal validation cohort: 5·3% [95% CI 3·4–8·1] for phenotype A, 31·3% [28·5–34·2] for phenotype B, and 59·5% [48·8–69·3] for phenotype C; external validation cohort: 3·7% [2·0–6·4] for phenotype A, 23·7% [21·8–25·7] for phenotype B, and 51·4% [41·9–60·7] for phenotype C).

Interpretation: Patients admitted to hospital with COVID-19 can be classified into three phenotypes that correlate with mortality. It was developed and validated a simplified tool for the probabilistic assignment of patients into phenotypes. These results might help to better classify patients for clinical management, but the pathophysiological mechanisms of the phenotypes must be investigated.

Reference

https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00019-0/fulltext

Publication Date: Feb 22, 2021

A public health approach for deciding policy on infant feeding and mother–infant contact in the context of COVID-19

Abstract

The COVID-19 pandemic has raised concern about the possibility and effects of mother–infant transmission of SARS-CoV-2 through breastfeeding and close contact. The insufficient available evidence has resulted in differing recommendations by health professional associations and national health authorities. An approach was presented

for deciding public health policy on infant feeding and mother–infant contact in the context of COVID-19, or for future emerging viruses, that balances the risks that are associated with viral infection against child survival, lifelong health, and development, and also maternal health. Using the Lives Saved Tool, we used available data to show how different public health approaches might affect infant mortality. Based on existing evidence, including population and survival estimates, the number of infant deaths in low-income and middle-income countries due to COVID-19 (2020–21) might range between 1800 and 2800. By contrast, if mothers with confirmed SARS-CoV-2 infection are recommended to separate from their newborn babies and avoid or stop breastfeeding, additional deaths among infants would range between 188 000 and 273 000.

Reference

https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(20)30538-6/fulltext

Medical vulnerability of individuals with Down syndrome to severe COVID-19–data from the Trisomy 21 Research Society and the UK ISARIC4C survey

Abstract

Background: Health conditions, immune dysfunction, and premature aging associated with trisomy 21 (Down syndrome, DS) may impact the clinical course of COVID-19.

Methods: The T21RS COVID-19 Initiative launched an international survey for clinicians or caregivers on patients with COVID-19 and DS. Data collected between April and October 2020 (N=1046) were analysed and compared with the UK ISARIC4C survey of hospitalized COVID-19 patients with and without DS.

Findings: The mean age of COVID-19 patients with DS in the T21RS survey was 29 years (SD = 18). Similar to the general population, the most frequent signs and symptoms of COVID-19 were fever, cough, and shortness of breath. Joint/muscle pain and vomiting or nausea were less frequent ($p < 0.01$), whereas altered consciousness/confusion were more frequent ($p < 0.01$). Risk factors for hospitalization and mortality were similar to the general population with the addition of congenital heart defects as a risk factor for hospitalization. Mortality rates showed a rapid increase from age 40 and were higher in patients with DS (T21RS DS versus non-DS patients: risk

ratio (RR) = 3.5 (95%-CI=2.6;4.4), ISARIC4C DS versus non-DS patients: RR = 2.9 (95%-CI=2.1;3.8)) even after adjusting for known risk factors for COVID-19 mortality.

Interpretation: Leading signs/symptoms of COVID-19 and risk factors for severe disease course are similar to the general population. However, individuals with DS present significantly higher rates of medical complications and mortality, especially from age 40.

Reference

https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00049-3/fulltext

Protein/AS01B vaccination elicits stronger, more Th2-skewed antigen-specific human T follicular helper cell responses than heterologous viral vectors

Abstract

Interactions between B cells and CD4+ T follicular helper (Tfh) cells are key determinants of humoral responses. Using samples from clinical trials performed with the malaria vaccine candidate antigen Plasmodium falciparum merozoite protein (PfRH5), we compare the frequency, phenotype, and gene expression profiles of PfRH5-specific circulating Tfh (cTfh) cells elicited by two leading human vaccine delivery platforms: heterologous viral vector prime boost and protein with AS01B adjuvant. We demonstrate that the protein/AS01B platform induces a higher-magnitude antigen-specific cTfh cell response and that this correlates with peak anti-PfRH5 IgG concentrations, frequency of PfRH5-specific memory B cells, and antibody functionality. Furthermore, the data indicated a greater Th2/Tfh2 skew within the polyfunctional response elicited following vaccination with protein/AS01B as compared to a Th1/Tfh1 skew with viral vectors. These data highlight the impact of vaccine platform on the cTfh cell response driving humoral immunity, associating a high-magnitude, Th2-biased cTfh response with potent antibody production.

Reference

https://www.cell.com/cell-reports-medicine/fulltext/S2666-3791(21)00018-5

Modeling COVID-19 epidemics in an Excel spreadsheet to enable first-hand accurate predictions of the pandemic evolution in urban areas

Abstract

COVID-19, the first pandemic of this decade and the second in less than 15 years, has harshly taught us that viral diseases do not recognize boundaries; however, they truly do discriminate between aggressive and mediocre containment responses. We present a simple epidemiological model that is amenable to implementation in Excel spreadsheets and sufficiently accurate to reproduce observed data on the evolution of the COVID-19 pandemics in different regions [*i.e.*, New York City (NYC), South Korea, Mexico City]. It was shown that the model can be adapted to closely follow the evolution of COVID-19 in any large city by simply adjusting parameters related to demographic conditions and aggressiveness of the response from a society/government to epidemics. Moreover, it was shown that this simple epidemiological simulator can be used to assess the efficacy of the response of a government/society to an outbreak. The simplicity and accuracy of this model will greatly contribute to democratizing the availability of knowledge in societies regarding the extent of an epidemic event and the efficacy of a governmental response.

Reference

https://www.nature.com/articles/s41598-021-83697-w

Correlation between early features and prognosis of symptomatic COVID-19 discharged patients in Hunan, China

Abstract

To determine the correlation between the clinical, laboratory, and radiological findings and the hospitalization days in Coronavirus Infectious Disease-19 (COVID-19) discharged patients. We retrospectively identified 172 discharged patients with COVID-19 pneumonia from January 10, 2020, to February 28, 2020, in Hunan province. The patients were categorized into group 1 (≤ 19 days) and group 2 (> 19 days) based on the time from symptom onset to discharge. Cough during admission occurred more commonly in group 2 (68.4%) than in group 1 (53.1%, $p = 0.042$). White blood cell ($p = 0.045$), neutrophil counts ($p = 0.023$), Alanine aminotransferase ($p = 0.029$),

Aspartate aminotransferase ($p = 0.027$) and Lactate dehydrogenase ($p = 0.021$) that were above normal were more common in group 2. Patients with single lesions were observed more in group 1(17.7%, $p = 0.018$) and multiple lesions observed more in group 2(86.8%, $p = 0.012$). The number of lobes involved ($p = 0.008$) in the CT score ($p = 0.001$) for each patient was all differences between the two groups with a statistically significant difference. Mixed ground-glass opacity (GGO) and consolidation appearances were observed in most patients. GGO components > consolidation appearance was more common in group 1 (25.0%) than in group 2 (8.0%) with a significant difference (0.015), GGO < consolidation was more common in group 2(71.1%, $p = 0.012$). From the logistic regression analysis, the CT score (OR, 1.223; 95% CI, 1.004 to 1.491, $p = 0.046$) and the appearance of GGO > consolidation (OR, 0.150; 95% CI, 0.034 to 0.660, $p = 0.012$) were independently associated with the hospitalization days. Thus, special attention should be paid to the role of radiological features in monitoring the disease prognosis.

Reference

https://www.nature.com/articles/s41598-021-83654-7

Antibody affinity maturation and plasma IgA associate with clinical outcome in hospitalized COVID-19 patients

Abstract

Hospitalized COVID-19 patients often present with a large spectrum of clinical symptoms. There is a critical need to better understand the immune responses to SARS-CoV-2 that lead to either resolution or exacerbation of the clinical disease. Here, longitudinal plasma samples were examined from hospitalized COVID-19 patients with differential clinical outcome. Immune-repertoire analysis were performed including cytokine, hACE2-receptor inhibition, neutralization titers, antibody epitope repertoire, antibody kinetics, antibody isotype and antibody affinity maturation against the SARS-CoV-2 prefusion spike protein. Fatal cases demonstrate high plasma levels of IL-6, IL-8, TNFα, and MCP-1, and sustained high percentage of IgA-binding antibodies to prefusion spike compared with non-ICU survivors. Disease resolution in non-ICU and ICU patients associates with antibody binding to the receptor binding motif and fusion peptide, and antibody affinity maturation to SARS-CoV-2 prefusion spike protein. Here,

an insight was provided into the immune parameters associated with clinical disease severity and disease-resolution outcome in hospitalized patients that could inform development of vaccine/therapeutics against COVID-19.

Reference

https://www.nature.com/articles/s41467-021-21463-2

Digital PCR for high sensitivity viral detection in false-negative SARS-CoV-2 patients

Abstract

Patients requiring diagnostic testing for coronavirus disease 2019 (COVID-19) are routinely assessed by reverse-transcription quantitative polymerase chain reaction (RT-qPCR) amplification of Sars-CoV-2 virus RNA extracted from oro/nasopharyngeal swabs. Despite the good specificity of the assays certified for SARS-CoV-2 molecular detection, and a theoretical sensitivity of few viral gene copies per reaction, a relatively high rate of false negatives continues to be reported. This is an important challenge in the management of patients on hospital admission and for correct monitoring of the infectivity after the acute phase. In the present report, it was shown that the use of digital PCR, a high sensitivity method to detect low amplicon numbers, allowed us to correctly detecting infection in swab material in a significant number of false negatives. It was shown that the implementation of digital PCR methods in the diagnostic assessment of COVID-19 could resolve, at least in part, this timely issue.

Reference

https://www.nature.com/articles/s41598-021-83723-x

SARS-CoV-2 vaccines strategies: A comprehensive review of phase 3 candidates

Abstract

The new SARS-CoV-2 virus is an RNA virus that belongs to the Coronaviridae family and causes COVID-19 disease. The newly sequenced virus appears to originate in China and rapidly spread throughout the world, becoming a pandemic that, until January 5th, 2021, has caused more than 1,866,000 deaths. Hence, laboratories worldwide are developing an effective vaccine against this disease, which will be

essential to reduce morbidity and mortality. Currently, there more than 64 vaccine candidates, most of them aiming to induce neutralizing antibodies against the spike protein (S). These antibodies will prevent uptake through the human ACE-2 receptor, thereby limiting viral entrance. Different vaccine platforms are being used for vaccine development, each one presenting several advantages and disadvantages. Thus far, thirteen vaccine candidates are being tested in Phase 3 clinical trials; therefore, it is closer to receiving approval or authorization for large-scale immunizations.

Reference

https://www.nature.com/articles/s41541-021-00292-w

Efficacy and safety of systematic corticosteroids among severe COVID-19 patients: A systematic review and meta-analysis of randomized controlled trials

Abstract

The benefits and harms of corticosteroids for patients with severe coronavirus disease 2019 (COVID-19) remain unclear. It was systematically searched PubMed, Embase, and Cochrane Central Register of Controlled Trials from December 31, 2019 to October 1, 2020 to identify randomized controlled trials (RCTs) that evaluated corticosteroids in severe COVID-19 patients. The primary outcome was all-cause mortality at the longest follow-up. Secondary outcomes included a composite disease progression (progression to intubation, ventilation, extracorporeal membrane oxygenation, ICU transfer, or death among those not ventilated at enrollment) and incidence of serious adverse events. A random-effects model was applied to calculate risk ratio (RR) with 95% confidence intervals (CIs). Grading of Recommendations Assessment, Development, and Evaluation approach was used to evaluate the certainty of the evidence. Seven RCTs involving 6250 patients were included, of which the Randomized Evaluation of COVID-19 Therapy (RECOVERY) trial comprised nearly 78% of all included subjects. Results showed that corticosteroids were associated with a decreased all-cause mortality (27.3 vs. 31.1%; RR: 0.85; 95% CI: 0.73–0.99; $P = 0.04$; low-certainty evidence). Trial sequential analysis suggested that more trials were still required to confirm the results. However, such survival benefit was absent if RECOVERY trial was excluded (RR: 0.83; 95% CI: 0.65–1.06; $P = 0.13$). Furthermore, corticosteroids decreased the occurrence of composite disease progression (30.6 vs. 33.3%; RR: 0.77; 95% CI: 0.64–

0.92; *P* = 0.005), but not increased the incidence of serious adverse events (3.5 vs. 3.4%; RR: 1.16; 95% CI: 0.39–3.43; *P* = 0.79).

Reference

https://www.nature.com/articles/s41392-021-00521-7

Serine 477 plays a crucial role in the interaction of the SARS-CoV-2 spike protein with the human receptor ACE2

Abstract

Since the worldwide outbreak of the infectious disease COVID-19, several studies have been published to understand the structural mechanism of the novel coronavirus SARS-CoV-2. During the infection process, the SARS-CoV-2 spike (S) protein plays a crucial role in the receptor recognition and cell membrane fusion process by interacting with the human angiotensin-converting enzyme 2 (hACE2) receptor. However, new variants of these spike proteins emerge as the virus passes through the disease reservoir. This poses a major challenge for designing a potent antigen for an effective immune response against the spike protein. Through a normal mode analysis (NMA) we identified the highly flexible region in the receptor binding domain (RBD) of SARS-CoV-2, starting from residue 475 up to residue 485. Structurally, the position S477 shows the highest flexibility among them. At the same time, S477 is hitherto the most frequently exchanged amino acid residue in the RBDs of SARS-CoV-2 mutants. Therefore, using MD simulations, we have investigated the role of S477 and its two frequent mutations (S477G and S477N) at the RBD during the binding to hACE2. We found that the amino acid exchanges S477G and S477N strengthen the binding of the SARS-COV-2 spike with the hACE2 receptor.

Reference

https://www.nature.com/articles/s41598-021-83761-5

In silico detection of SARS-CoV-2 specific B-cell epitopes and validation in ELISA for serological diagnosis of COVID-19

Abstract

Rapid generation of diagnostics is paramount to understand epidemiology and to control the spread of emerging infectious diseases such as COVID-19. Computational methods to predict serodiagnostic epitopes that are specific for the pathogen could help accelerate the development of new diagnostics. A systematic survey of 27 SARS-CoV-2 proteins was conducted to assess whether existing B-cell epitope prediction methods, combined with comprehensive mining of sequence databases and structural data, could predict whether a particular protein would be suitable for serodiagnosis. Nine of the predictions were validated with recombinant SARS-CoV-2 proteins in the ELISA format using plasma and sera from patients with SARS-CoV-2 infection, and a further 11 predictions were compared to the recent literature. Results appeared to be in agreement with 12 of the predictions, in disagreement with 3, while a further 5 were deemed inconclusive. We showed that two of our top five candidates, the N-terminal fragment of the nucleoprotein and the receptor-binding domain of the spike protein, have the highest sensitivity and specificity and signal-to-noise ratio for detecting COVID-19 sera/plasma by ELISA. Mixing the two antigens together for coating ELISA plates led to a sensitivity of 94% (N = 80 samples from persons with RT-PCR confirmed SARS-CoV-2 infection), and a specificity of 97.2% (N = 106 control samples).

Reference

https://www.nature.com/articles/s41598-021-83730-y

Publication Date: Feb 19, 2021

Single-dose administration and the influence of the timing of the booster dose on immunogenicity and efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine: A pooled analysis of four randomised trials

Abstract

Background: The ChAdOx1 nCoV-19 (AZD1222) vaccine has been approved for emergency use by the UK regulatory authority, Medicines and Healthcare products Regulatory Agency, with a regimen of two standard doses given with an interval of 4–12

weeks. The planned roll-out in the UK will involve vaccinating people in high-risk categories with their first dose immediately, and delivering the second dose 12 weeks later. Here, a further prespecified pooled analysis of trials of ChAdOx1 nCoV-19 was provided as well as exploratory analyses of the impact on immunogenicity and efficacy of extending the interval between priming and booster doses. In addition, we show the immunogenicity and protection afforded by the first dose, before a booster dose has been offered.

Methods: Data was presented from three single-blind randomised controlled trials—one phase 1/2 study in the UK (COV001), one phase 2/3 study in the UK (COV002), and a phase 3 study in Brazil (COV003)—and one double-blind phase 1/2 study in South Africa (COV005). As previously described, individuals 18 years and older were randomly assigned 1:1 to receive two standard doses of ChAdOx1 nCoV-19 (5 × 1010 viral particles) or a control vaccine or saline placebo. In the UK trial, a subset of participants received a lower dose (2·2 × 1010 viral particles) of the ChAdOx1 nCoV-19 for the first dose. The primary outcome was virologically confirmed symptomatic COVID-19 disease, defined as a nucleic acid amplification test (NAAT)-positive swab combined with at least one qualifying symptom (fever ≥37·8°C, cough, shortness of breath, or anosmia or ageusia) more than 14 days after the second dose. Secondary efficacy analyses included cases occuring at least 22 days after the first dose. Antibody responses measured by immunoassay and by pseudovirus neutralisation were exploratory outcomes. All cases of COVID-19 with a NAAT-positive swab were adjudicated for inclusion in the analysis by a masked independent endpoint review committee. The primary analysis included all participants who were SARS-CoV-2 N protein seronegative at baseline, had had at least 14 days of follow-up after the second dose, and had no evidence of previous SARS-CoV-2 infection from NAAT swabs. Safety was assessed in all participants who received at least one dose. The four trials are registered at ISRCTN89951424 (COV003) and ClinicalTrials.gov, NCT04324606 (COV001), NCT04400838 (COV002), and NCT04444674 (COV005).

Findings: Between April 23 and Dec 6, 2020, 24 422 participants were recruited and vaccinated across the four studies, of whom 17 178 were included in the primary analysis (8597 receiving ChAdOx1 nCoV-19 and 8581 receiving control vaccine). The data cutoff for these analyses was Dec 7, 2020. 332 NAAT-positive infections met the

primary endpoint of symptomatic infection more than 14 days after the second dose. Overall vaccine efficacy more than 14 days after the second dose was 66·7% (95% CI 57·4–74·0), with 84 (1·0%) cases in the 8597 participants in the ChAdOx1 nCoV-19 group and 248 (2·9%) in the 8581 participants in the control group. There were no hospital admissions for COVID-19 in the ChAdOx1 nCoV-19 group after the initial 21-day exclusion period, and 15 in the control group. 108 (0·9%) of 12 282 participants in the ChAdOx1 nCoV-19 group and 127 (1·1%) of 11 962 participants in the control group had serious adverse events. There were seven deaths considered unrelated to vaccination (two in the ChAdOx1 nCov-19 group and five in the control group), including one COVID-19-related death in one participant in the control group. Exploratory analyses showed that vaccine efficacy after a single standard dose of vaccine from day 22 to day 90 after vaccination was 76·0% (59·3–85·9). Our modelling analysis indicated that protection did not wane during this initial 3-month period. Similarly, antibody levels were maintained during this period with minimal waning by day 90 (geometric mean ratio [GMR] 0·66 [95% CI 0·59–0·74]). In the participants who received two standard doses, after the second dose, efficacy was higher in those with a longer prime-boost interval (vaccine efficacy 81·3% [95% CI 60·3–91·2] at ≥12 weeks) than in those with a short interval (vaccine efficacy 55·1% [33·0–69·9] at <6 weeks). These observations are supported by immunogenicity data that showed binding antibody responses more than two-fold higher after an interval of 12 or more weeks compared with an interval of less than 6 weeks in those who were aged 18–55 years (GMR 2·32 [2·01–2·68]).

Interpretation: The results of this primary analysis of two doses of ChAdOx1 nCoV-19 were consistent with those seen in the interim analysis of the trials and confirm that the vaccine is efficacious, with results varying by dose interval in exploratory analyses. A 3-month dose interval might have advantages over a programme with a short dose interval for roll-out of a pandemic vaccine to protect the largest number of individuals in the population as early as possible when supplies are scarce, while also improving protection after receiving a second dose.

Reference

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00432-3/fulltext

Cyclin-dependent kinases as emerging targets for developing novel antiviral therapeutics

Abstract

Drug repurposing is an effective strategy to develop new antiviral therapies as the identification of new uses for already approved drugs is highly efficient, time-saving, cost-effective, and minimizes the risk of failure, while maximizing the therapeutic value of a drug. Viruses use a variety of strategies to usurp and control cellular activities, with the manipulation of the host cell cycle being one of the most frequent. Meeting the timely clinical needs presented by emerging viruses will be best achieved by the development of broad-spectrum antiviral therapies that target enzymatic functions shared by multiple viruses and the host–cell machinery, such as cell cycle control through modification of CDK function. The advent of novel specific CDK inhibitors with better toxicity profiles in cancer clinical trials, together with accumulating preclinical data that shed light on the antiviral and immunomodulatory properties of CDK inhibitors, opens new avenues to enable the rapid development of a new class of broad-spectrum antivirals.

Besides its prominent role in cell proliferation, cyclin-dependent kinases (CDKs) are key players in viral infections as both DNA and RNA viruses modify CDK function to favor viral replication. Recently, a number of specific pharmacological CDK inhibitors have been developed and approved for cancer treatment. The repurposing of these specific CDK inhibitors for the treatment of viral infections may represent a novel effective therapeutic strategy to combat old and emergent viruses. In this review, the role, mechanisms of action, and potential of CDKs as antiviral drug targets were described. The current clinical state of novel specific CDK inhibitors was also discussed, focusing on their putative use as antivirals, especially against new emerging viruses.

Reference

https://www.cell.com/trends/microbiology/fulltext/S0966-842X(21)00016-0

COVID-19—from mucosal immunology to IBD patients

Abstract

Viral infections with SARS-CoV-2 can cause a multi-facetted disease, which is not only characterized by pneumonia and overwhelming systemic inflammatory immune responses, but which can also directly affect the digestive system and infect intestinal epithelial cells. Here, the current understanding of intestinal tropism of SARS-CoV-2 infection was reviewed, its impact on mucosal function and immunology and summarize the effect of immune-suppression in patients with inflammatory bowel disease (IBD) on disease outcome of COVID-19 and discuss IBD-relevant implications for the clinical management of SARS-CoV-2 infected individuals.

Reference

https://www.nature.com/articles/s41385-021-00384-9

Harnessing peak transmission around symptom onset for non-pharmaceutical intervention and containment of the COVID-19 pandemic

Abstract

Within a short period of time, COVID-19 grew into a world-wide pandemic. Transmission by pre-symptomatic and asymptomatic viral carriers rendered intervention and containment of the disease extremely challenging. Based on reported infection case studies, an epidemiological model was constructed that focuses on transmission around the symptom onset. The model is calibrated against incubation period and pairwise transmission statistics during the initial outbreaks of the pandemic outside Wuhan with minimal non-pharmaceutical interventions. Mathematical treatment of the model yields explicit expressions for the size of latent and pre-symptomatic subpopulations during the exponential growth phase, with the local epidemic growth rate as input. Reduction of the basic reproduction number R_0 was then explored through specific transmission control measures such as contact tracing, testing, social distancing, wearing masks and sheltering in place. When these measures are implemented in combination, their effects on R_0 multiply. The model behaviour was also compared to the first wave of the COVID-19 spreading in various affected regions and highlight generic and less generic features of the pandemic development.

Reference

https://www.nature.com/articles/s41467-021-21385-z

Evolution of immune responses to SARS-CoV-2 in mild-moderate COVID-19

Abstract

The durability of infection-induced SARS-CoV-2 immunity has major implications for reinfection and vaccine development. Here, a comprehensive profile of antibody, B cell and T cell dynamics was shown over time in a cohort of patients who have recovered from mild-moderate COVID-19. Binding and neutralising antibody responses, together with individual serum clonotypes, decay over the first 4 months post-infection. A similar decline in Spike-specific CD4+ and circulating T follicular helper frequencies occurs. By contrast, S-specific IgG+ memory B cells consistently accumulate over time, eventually comprising a substantial fraction of circulating the memory B cell pool. Modelling of the concomitant immune kinetics predicts maintenance of serological neutralising activity above a titre of 1:40 in 50% of convalescent participants to 74 days, although there is probably additive protection from B cell and T cell immunity. This study indicates that SARS-CoV-2 immunity after infection might be transiently protective at a population level. Therefore, SARS-CoV-2 vaccines might require greater immunogenicity and durability than natural infection to drive long-term protection.

Reference

https://www.nature.com/articles/s41467-021-21444-5

Positive effects of COVID-19 lockdown on air quality of industrial cities (Ankleshwar and Vapi) of Western India

Abstract

On January 30, 2020, India recorded its first COVID-19 positive case in Kerala, which was followed by a nationwide lockdown extended in four different phases from 25th March to 31st May, 2020, and an unlock period thereafter. The lockdown has led to colossal economic loss to India; however, it has come as a respite to the environment. Utilizing the air quality index (AQI) data recorded during this adverse time, the present study is undertaken to assess the impact of lockdown on the air quality of Ankleshwar and Vapi, Gujarat, India. The AQI data obtained from the Central Pollution Control

Board was assessed for four lockdown phases. We compared air quality data for the unlock phase with a coinciding period in 2019 to determine the changes in pollutant concentrations during the lockdown, analyzing daily AQI data for six pollutants (PM10, PM2.5, CO, NO_2, O_3, and SO_2). A meta-analysis of continuous data was performed to determine the mean and standard deviation of each lockdown phase, and their differences were computed in percentage in comparison to 2019; along with the linear correlation analysis and linear regression analysis to determine the relationship among the air pollutants and their trend for the lockdown days. The results revealed different patterns of gradual to a rapid reduction in most of the pollutant concentrations (PM10, PM2.5, CO, SO2), and an increment in ozone concentration was observed due to a drastic reduction in NO_2 by 80.18%. Later, increases in other pollutants were also observed as the restrictions were eased during phase-4 and unlock 1. The comparison between the two cities found that factors like distance from the Arabian coast and different industrial setups played a vital role in different emission trends.

Reference

https://www.nature.com/articles/s41598-021-83393-9

Immune transcriptomes of highly exposed SARS-CoV-2 asymptomatic seropositive *versus* seronegative individuals from the Ischgl community

Abstract

SARS-CoV-2 infection ranges from asymptomatic to severe with lingering symptomatology in some. This prompted investigation of whether or not asymptomatic disease results in measurable immune activation post-infection. Immune activation following asymptomatic SARS-CoV-2 infection was characterized through a comparative investigation of the immune cell transcriptomes from 43 asymptomatic seropositive and 52 highly exposed seronegative individuals from the same community 4–6 weeks following a superspreading event. Few of the 95 individuals had underlying health issues. One seropositive individual reported Cystic Fibrosis and one individual reported Incontinentia pigmenti. No evidence of immune activation was found in asymptomatic seropositive individuals with the exception of the Cystic Fibrosis patient. There were no statistically significant differences in immune transcriptomes between asymptomatic seropositive and highly exposed seronegative individuals. Four positive

controls, mildly symptomatic seropositive individuals whose blood was examined 3 weeks following infection, showed immune activation. Negative controls were four seronegative individuals from neighboring communities without COVID-19. All individuals remained in their usual state of health through a five-month follow-up after sample collection. In summary, whole blood transcriptomes identified individual immune profiles within a community population and showed that asymptomatic infection within a super-spreading event was not associated with enduring immunological activation.

Reference

https://www.nature.com/articles/s41598-021-83110-6

Exploring beyond clinical routine SARS-CoV-2 serology using MultiCoV-Ab to evaluate endemic coronavirus cross-reactivity

Abstract

The humoral immune response to SARS-CoV-2 is a benchmark for immunity and detailed analysis is required to understand the manifestation and progression of COVID-19, monitor seroconversion within the general population, and support vaccine development. The majority of currently available commercial serological assays only quantify the SARS-CoV-2 antibody response against individual antigens, limiting the understanding of the immune response. To overcome this, a multiplex immunoassay (MultiCoV-Ab) was developed including spike and nucleocapsid proteins of SARS-CoV-2 and the endemic human coronaviruses. Compared to three broadly used commercial in vitro diagnostic tests, our MultiCoV-Ab achieves a higher sensitivity and specificity when analyzing a well-characterized sample set of SARS-CoV-2 infected and uninfected individuals. A high response was found against endemic coronaviruses in our sample set, but no consistent cross-reactive IgG response patterns against SARS-CoV-2. Here, a robust, high-content-enabled, antigen-saving multiplex assay was shown, suited to both monitoring vaccination studies and facilitating epidemiologic screenings for humoral immunity towards pandemic and endemic coronaviruses.

Reference

https://www.nature.com/articles/s41467-021-20973-3

Flexibility and mobility of SARS-CoV-2-related protein structures

Abstract

The worldwide CoVid-19 pandemic has led to an unprecedented push across the whole of the scientific community to develop a potent antiviral drug and vaccine as soon as possible. Existing academic, governmental and industrial institutions and companies have engaged in large-scale screening of existing drugs, in vitro, in vivo and in silico. Here, we are using in silico modelling of possible SARS-CoV-2 drug targets, as deposited on the Protein Databank (PDB), and ascertain their dynamics, flexibility and rigidity. For example, for the SARS-CoV-2 spike protein—using its complete homo-trimer configuration with 2905 residues—our method identifies a large-scale opening and closing of the S1 subunit through movement of the S^B domain. The full structural information of this process was computed, allowing for docking studies with possible drug structures. In a dedicated database, we present similarly detailed results for the further, nearly 300, thus far resolved SARS-CoV-2-related protein structures in the PDB.

Reference

https://www.nature.com/articles/s41598-021-82849-2

Publication Date: Feb 18, 2021

Indirect acute effects of the COVID-19 pandemic on physical and mental health in the UK: A population-based study

Background: There are concerns that the response to the COVID-19 pandemic in the UK might have worsened physical and mental health, and reduced use of health services. However, the scale of the problem is unquantified, impeding development of effective mitigations. We aimed to ascertain what has happened to general practice contacts for acute physical and mental health outcomes during the pandemic.

Methods: Using de-identified electronic health records from the Clinical Research Practice Datalink (CPRD) Aurum (covering 13% of the UK population), between 2017 and 2020, we calculated weekly primary care contacts for selected acute physical and mental health conditions: anxiety, depression, self-harm (fatal and non-fatal), severe mental illness, eating disorder, obsessive-compulsive disorder, acute alcohol-related events, asthma exacerbation, chronic obstructive pulmonary disease exacerbation,

acute cardiovascular events (cerebrovascular accident, heart failure, myocardial infarction, transient ischaemic attacks, unstable angina, and venous thromboembolism), and diabetic emergency. Primary care contacts included remote and face-to-face consultations, diagnoses from hospital discharge letters, and secondary care referrals, and conditions were identified through primary care records for diagnoses, symptoms, and prescribing. The overall study population included individuals aged 11 years or older who had at least 1 year of registration with practices contributing to CPRD Aurum in the specified period, but denominator populations varied depending on the condition being analysed. An interrupted time-series analysis was used to formally quantify changes in conditions after the introduction of population-wide restrictions (defined as March 29, 2020) compared with the period before their introduction (defined as Jan 1, 2017 to March 7, 2020), with data excluded for an adjustment-to-restrictions period (March 8–28).

Findings: The overall population included 9 863 903 individuals on Jan 1, 2017, and increased to 10 226 939 by Jan 1, 2020. Primary care contacts for almost all conditions dropped considerably after the introduction of population-wide restrictions. The largest reductions were observed for contacts for diabetic emergencies (odds ratio 0·35 [95% CI 0·25–0·50]), depression (0·53 [0·52–0·53]), and self-harm (0·56 [0·54–0·58]). In the interrupted time-series analysis, with the exception of acute alcohol-related events (0·98 [0·89–1·10]), there was evidence of a reduction in contacts for all conditions (anxiety 0·67 [0·66–0·67], eating disorders 0·62 [0·59–0·66], obsessive-compulsive disorder [0·69 [0·64–0·74]], self-harm 0·56 [0·54–0·58], severe mental illness 0·80 [0·78–0·83], stroke 0·59 [0·56–0·62], transient ischaemic attack 0·63 [0·58–0·67], heart failure 0·62 [0·60–0·64], myocardial infarction 0·72 [0·68–0·77], unstable angina 0·72 [0·60–0·87], venous thromboembolism 0·94 [0·90–0·99], and asthma exacerbation 0·88 [0·86–0·90]). By July, 2020, except for unstable angina and acute alcohol-related events, contacts for all conditions had not recovered to pre-lockdown levels.

Interpretation: There were substantial reductions in primary care contacts for acute physical and mental conditions following the introduction of restrictions, with limited recovery by July, 2020. Further research is needed to ascertain whether these reductions reflect changes in disease frequency or missed opportunities for care. Maintaining health-care access should be a key priority in future public health planning,

including further restrictions. The conditions we studied are sufficiently severe that any unmet need will have substantial ramifications for the people with the conditions as well as health-care provision.

Reference

https://www.thelancet.com/journals/landig/article/PIIS2589-7500(21)00017-0/fulltext

The antigenic anatomy of SARS-CoV-2 receptor binding domain

Abstract

SARS-CoV-2 has caused over 2M deaths in little over a year. Vaccines are being deployed at scale, aiming to generate responses against the virus spike. The scale of the pandemic and error-prone virus replication is leading to the appearance of mutant viruses and potentially escape from antibody responses. Variant B.1.1.7, now dominant in the UK, with increased transmission, harbours 9 amino-acid changes in the spike, including N501Y in the ACE2 interacting-surface. The ability of B.1.1.7 to evade antibody responses was examined, elicited by natural SARS-CoV-2 infection or vaccination. The impact of N501Y by structure/function analysis of a large panel of well-characterised monoclonal antibodies was mapped. B.1.1.7 is harder to neutralize than parental virus, compromising neutralization by some members of a major class of public antibodies through light chain contacts with residue 501. However, widespread escape from monoclonal antibodies or antibody responses generated by natural infection or vaccination was not observed.

Reference

https://www.cell.com/cell/fulltext/S0092-8674(21)00222-1

The antigenic anatomy of SARS-CoV-2 receptor binding domain

Abstract

Antibodies are crucial to immune protection against SARS-CoV-2, with some in emergency use as therapeutics. Here 377 human monoclonal antibodies (mAbs) were identified recognizing the virus spike, and focus mainly on 80 that bind the receptor binding domain (RBD). A competition data driven method was devised to map RBD binding sites. It was found that although antibody binding sites are widely dispersed,

neutralizing antibody binding is focused, with nearly all highly inhibitory mAbs (IC50<0.1μg/ml) blocking receptor interaction, except for one that binds a unique epitope in the N-terminal domain. Many of these neutralizing mAbs use public V-genes and are close to germline. The structural basis of recognition was dissected for this large panel of antibodies through X-ray crystallography and cryo-electron microscopy of 19 Fab-antigen structures. Novel binding modes were found for some potently inhibitory antibodies and demonstrate that strongly neutralizing mAbs protect, prophylactically or therapeutically, in animal models.

Reference

https://www.cell.com/cell/fulltext/S0092-8674(21)00221-X

Interleukin-3 is a predictive marker for severity and outcome during SARS-CoV-2 infections

Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a worldwide health threat. In a prospective multicentric study, we identify IL-3 as an independent prognostic marker for the outcome during SARS-CoV-2 infections. Specifically, low plasma IL-3 levels is associated with increased severity, viral load, and mortality during SARS-CoV-2 infections. Patients with severe COVID-19 exhibit also reduced circulating plasmacytoid dendritic cells (pDCs) and low plasma IFNα and IFNλ levels when compared to non-severe COVID-19 patients. In a mouse model of pulmonary HSV-1 infection, treatment with recombinant IL-3 reduces viral load and mortality. Mechanistically, IL-3 increases innate antiviral immunity by promoting the recruitment of circulating pDCs into the airways by stimulating CXCL12 secretion from pulmonary CD123+ epithelial cells, both, in mice and in COVID-19 negative patients exhibiting pulmonary diseases. This study identifies IL-3 as a predictive disease marker for SARS-CoV-2 infections and as a potential therapeutic target for pulmunory viral infections.

Reference

https://www.nature.com/articles/s41467-021-21310-4

Massively parallel assessment of human variants with base editor screens

Abstract

Understanding the functional consequences of single-nucleotide variants is critical to uncovering the genetic underpinnings of diseases, but technologies to characterize variants are limiting. Here, CRISPR-Cas9 cytosine base editors were leveraged in pooled screens to scalably assay variants at endogenous loci in mammalian cells. We benchmark the performance of base editors in positive and negative selection screens, identifying known loss-of-function mutations in BRCA1 and BRCA2 with high precision. To demonstrate the utility of base editor screens to probe small molecule-protein interactions against BH3 mimetics and PARP inhibitors were screened, identifying point mutations that confer drug sensitivity or resistance. a library of single guide RNAs (sgRNAs) was also created, predicted to generate 52,034 ClinVar variants in 3,584 genes and conduct screens in the presence of cellular stressors, identifying loss-of-function variants in numerous DNA damage repair genes. It was anticipated that this screening approach will be broadly useful to readily and scalably functionalize genetic variants.

Reference

https://www.cell.com/cell/fulltext/S0092-8674(21)00012-X

Extensions of the SEIR model for the analysis of tailored social distancing and tracing approaches to cope with COVID-19

Abstract

In the context of the COVID-19 pandemic, governments worldwide face the challenge of designing tailored measures of epidemic control to provide reliable health protection while allowing societal and economic activity. In this paper, an extension of the epidemiological SEIR model was proposed to enable a detailed analysis of commonly discussed tailored measures of epidemic control—among them group-specific protection and the use of tracing apps. Groups were introduced into the SEIR model that may differ both in their underlying parameters as well as in their behavioral response to public health interventions. Moreover, it was allowed for different infectiousness parameters within and across groups, different asymptomatic,

hospitalization, and lethality rates, as well as different take-up rates of tracing apps. We then examine predictions from these models for a variety of scenarios. The results visualize the sharp trade-offs between different goals of epidemic control, namely a low death toll, avoiding overload of the health system, and a short duration of the epidemic. We show that a combination of tailored mechanisms, e.g., the protection of vulnerable groups together with a “trace & isolate” approach, can be effective in preventing a high death toll. Protection of vulnerable groups without further measures requires unrealistically strict isolation. A key insight is that high compliance is critical for the effectiveness of a “trace & isolate” approach. The model allows to analyze the interplay of group-specific social distancing and tracing also beyond our case study in scenarios with a large number of groups reflecting, e.g., sectoral, regional, or age differentiation and group-specific behavioural responses.

Reference

https://www.nature.com/articles/s41598-021-83540-2

Coinfection with influenza A virus enhances SARS-CoV-2 infectivity

Abstract

The upcoming flu season in the Northern Hemisphere merging with the current COVID-19 pandemic raises a potentially severe threat to public health. Through experimental coinfection with influenza A virus (IAV) and either pseudotyped or live SARS-CoV-2 virus, IAV preinfection was found significantly promoted the infectivity of SARS-CoV-2 in a broad range of cell types. Remarkably, *in vivo*, increased SARS-CoV-2 viral load and more severe lung damage were observed in mice coinfected with IAV. Moreover, such enhancement of SARS-CoV-2 infectivity was not observed with several other respiratory viruses, likely due to a unique feature of IAV to elevate ACE2 expression. This study illustrates that IAV has a unique ability to aggravate SARS-CoV-2 infection, and thus, prevention of IAV infection is of great significance during the COVID-19 pandemic.

Reference

https://www.nature.com/articles/s41422-021-00473-1

Molecular features similarities between SARS-CoV-2, SARS, MERS and key human genes could favour the viral infections and trigger collateral effects

Abstract

In December 2019, rising pneumonia cases caused by a novel β-coronavirus (SARS-CoV-2) occurred in Wuhan, China, which has rapidly spread worldwide, causing thousands of deaths. The WHO declared the SARS-CoV-2 outbreak as a public health emergency of international concern, since then several scientists are dedicated to its study. It has been observed that many human viruses have codon usage biases that match highly expressed proteins in the tissues they infect and depend on the host cell machinery for the replication and co-evolution. In this work, 91 molecular features and codon usage patterns were analysed for 339 viral genes and 463 human genes that consisted of 677,873 codon positions. Hereby, the highly expressed genes were selected from human lung tissue to perform computational studies that permit to compare their molecular features with those of SARS, SARS-CoV-2 and MERS genes. The integrated analysis of all the features revealed that certain viral genes and overexpressed human genes have similar codon usage patterns. The main pattern was the A/T bias that together with other features could propitiate the viral infection, enhanced by a host dependant specialization of the translation machinery of only some of the overexpressed genes. The envelope protein E, the membrane glycoprotein M and ORF7 could be further benefited. This could be the key for a facilitated translation and viral replication conducting to different comorbidities depending on the genetic variability of population due to the host translation machinery. This is the first codon usage approach that reveals which human genes could be potentially deregulated due to the codon usage similarities between the host and the viral genes when the virus is already inside the human cells of the lung tissues. The work leaded to the identification of additional highly expressed human genes which are not the usual suspects but might play a role in the viral infection and settle the basis for further research in the field of human genetics associated with new viral infections. To identify the genes that could be deregulated under a viral infection is important to predict the collateral effects and determine which individuals would be more susceptible based on their genetic features and comorbidities associated.

Reference

https://www.nature.com/articles/s41598-021-83595-1

Key factors leading to fatal outcomes in COVID-19 patients with cardiac injury

Abstract

Cardiac injury among patients with COVID-19 has been reported and is associated with a high risk of mortality, but cardiac injury may not be the leading factor related to death. The factors related to poor prognosis among COVID-19 patients with myocardial injury are still unclear. This study aimed to explore the potential key factors leading to in-hospital death among COVID-19 patients with cardiac injury. This retrospective single-center study was conducted at Renmin Hospital of Wuhan University, from January 20, 2020 to April 10, 2020, in Wuhan, China. All inpatients with confirmed COVID-19 (≥ 18 years old) and cardiac injury who had died or were discharged by April 10, 2020 were included. Demographic data and clinical and laboratory findings were collected and compared between survivors and nonsurvivors. Univariable and multivariable logistic regression methods were used to explore the risk factors associated with mortality in COVID-19 patients with cardiac injury. A total of 173 COVID-19 patients with cardiac injury were included in this study, 86 were discharged and 87 died in the hospital. Multivariable regression showed increased odds of in-hospital death were associated with advanced age (odds ratio 1.12, 95% CI 1.05–1.18, per year increase; $p < 0.001$), coagulopathy (2.54, 1.26–5.12; $p = 0{\cdot}009$), acute respiratory distress syndrome (16.56, 6.66–41.2; $p < 0.001$), and elevated hypersensitive troponin I (4.54, 1.79–11.48; $p = 0.001$). A high risk of in-hospital death was observed among COVID-19 patients with cardiac injury in this study. The factors related to death include advanced age, coagulopathy, acute respiratory distress syndrome and elevated levels of hypersensitive troponin I.

Reference

https://www.nature.com/articles/s41598-021-82396-w

Early risk assessment for COVID-19 patients from emergency department data using machine learning

Abstract

Since its emergence in late 2019, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has caused a pandemic with more than 55 million reported cases and 1.3 million estimated deaths worldwide. While epidemiological and clinical characteristics of COVID-19 have been reported, risk factors underlying the transition from mild to severe disease among patients remain poorly understood. In this retrospective study, we analysed data of 879 confirmed SARS-CoV-2 positive patients admitted to a two-site NHS Trust hospital in London, England, between January 1st and May 26th, 2020, with a majority of cases occurring in March and April. We extracted anonymised demographic data, physiological clinical variables and laboratory results from electronic healthcare records (EHR) and applied multivariate logistic regression, random forest and extreme gradient boosted trees. To evaluate the potential for early risk assessment, we used data available during patients' initial presentation at the emergency department (ED) to predict deterioration to one of three clinical endpoints in the remainder of the hospital stay: admission to intensive care, need for invasive mechanical ventilation and in-hospital mortality. Based on the trained models, we extracted the most informative clinical features in determining these patient trajectories. Considering our inclusion criteria, we have identified 129 of 879 (15%) patients that required intensive care, 62 of 878 (7%) patients needing mechanical ventilation, and 193 of 619 (31%) cases of in-hospital mortality. The models learned successfully from early clinical data and predicted clinical endpoints with high accuracy, the best model achieving area under the receiver operating characteristic (AUC-ROC) scores of 0.76 to 0.87 (F1 scores of 0.42–0.60). Younger patient age was associated with an increased risk of receiving intensive care and ventilation, but lower risk of mortality. Clinical indicators of a patient's oxygen supply and selected laboratory results, such as blood lactate and creatinine levels, were most predictive of COVID-19 patient trajectories. Among COVID-19 patients machine learning can aid in the early identification of those with a poor prognosis, using EHR data collected during a patient's first presentation at ED. Patient age and measures of oxygenation status during ED stay are primary indicators of poor patient outcomes.

Reference

https://www.nature.com/articles/s41598-021-83784-y

Temporal association between human upper respiratory and gut bacterial microbiomes during the course of COVID-19 in adults

Abstract

SARS-CoV-2 is the cause of COVID-19. It infects multiple organs including the respiratory tract and gut. Dynamic changes of regional microbiomes in infected adults are largely unknown. Here, longitudinal analyses were performed of throat and anal swabs from 35 COVID-19 and 19 healthy adult controls, as well as 10 non-COVID-19 patients with other diseases, by 16 S rRNA gene sequencing. The results showed a partitioning of the patients into 3-4 categories based on microbial community types (I-IV) in both sites. The bacterial diversity was lower in COVID-19 patients than healthy controls and decreased gradually from community type I to III/IV. Although the dynamic change of microbiome was complex during COVID-19, a synchronous restoration of both the upper respiratory and gut microbiomes from early dysbiosis towards late more diverse status was observed in 6/8 mild COVID-19 adult patients. These findings reveal previously unknown interactions between upper respiratory and gut microbiomes during COVID-19.

Reference

https://www.nature.com/articles/s42003-021-01796-w

Assisting scalable diagnosis automatically via CT images in the combat against COVID-19

Abstract

The pandemic of Coronavirus Disease 2019 (COVID-19) is causing enormous loss of life globally. Prompt case identification is critical. The reference method is the real-time reverse transcription PCR (RT-PCR) assay, whose limitations may curb its prompt large-scale application. COVID-19 manifests with chest computed tomography (CT) abnormalities, some even before the onset of symptoms. We tested the hypothesis that the application of deep learning (DL) to 3D CT images could help identify COVID-19 infections. Using data from 920 COVID-19 and 1,073 non-COVID-19 pneumonia

patients, we developed a modified DenseNet-264 model, COVIDNet, to classify CT images to either class. When tested on an independent set of 233 COVID-19 and 289 non-COVID-19 pneumonia patients, COVIDNet achieved an accuracy rate of 94.3% and an area under the curve of 0.98. As of March 23, 2020, the COVIDNet system had been used 11,966 times with a sensitivity of 91.12% and a specificity of 88.50% in six hospitals with PCR confirmation. Application of DL to CT images may improve both efficiency and capacity of case detection and long-term surveillance.

Reference

https://www.nature.com/articles/s41598-021-83424-5

Mining Google and Apple mobility data: Temporal anatomy for COVID-19 social distancing

Abstract

The Google and Apple mobility data was employed to identify, quantify and classify different degrees of social distancing and characterise their imprint on the first wave of the COVID-19 pandemic in Europe and in the United States. The period of enacted social distancing were identified *via* Google and Apple data, independently from the political decisions. Our analysis allows us to classify different shades of social distancing measures for the first wave of the pandemic. A strong decrease in the infection rate was observed occurring two to five weeks after the onset of mobility reduction. A universal time scale emerges, after which social distancing shows its impact. An actual measure of the impact of social distancing for each region was further provided, showing that the effect amounts to a reduction by 20–40% in the infection rate in Europe and 30–70% in the US.

Reference

https://www.nature.com/articles/s41598-021-83441-4

Acute psychological impact on COVID-19 patients in Hubei: A multicenter observational study

Abstract

A multicentre cross-sectional survey of COVID-19 patients was conducted to evaluate the acute psychological impact on the patients with coronavirus disease 2019 (COVID-19) during isolation treatment based on online questionnaires from 2 February to 5 March 2020. A total of 460 COVID-19 patients from 13 medical centers in Hubei province were investigated for their mental health status using online questionnaires (including Patient Health Questionnaire-9, Generalized Anxiety Disorder-7, Patient Health Questionnaire-15, and Insomnia Severity Index scales). Among all 460 COVID-19 patients, 187 (40.65%) of them were healthcare workers (HCWs). 297 (64.57%) of them were females. The most common psychological problems were somatization symptoms (66.09%, n = 304), followed by depression (53.48%, n = 246), anxiety (46.30%, n = 213), problems of insomnia (42.01%, n = 171), and then self-mutilating or suicidal thoughts (23.26%, n = 107). Of all the patients, 15.65% (n = 72) had severe somatization symptoms, and 2.83% (n = 13) had severe (almost every day) self-mutilating or suicidal thoughts. The most common psychological problems for HCWs were somatization symptoms (67.84%, n = 125), followed by depression (51.87%, n = 97), anxiety (44.92%, n = 84), problems of insomnia (36.18%, n = 55), and then self-mutilating or suicidal thoughts (20.86%, n = 39). Patients with lower education levels were found to be associated with higher incidence of self-mutilating or suicidal thoughts (odds ratio [OR], 2.68, 95% confidence interval [95% CI], 1.66–4.33 [P < 0.001]). Patients with abnormal body temperature were found to be associated with higher incidence of self-mutilating or suicidal thoughts (OR, 3.97, 95% CI, 2.07–7.63 [P < 0.001]), somatic symptoms (OR, 2.06, 95% CI, 1.20–3.55 [P = 0.009]) and insomnia (OR, 1.66, 95% CI, 1.04–2.65 [P = 0.033]). Those with suspected infected family members displayed a higher prevalence of anxiety than those without infected family members (OR, 1.61, 95% CI, 1.1–2.37 [P = 0.015]). Patients at the age of 18–44 years old had fewer somatic symptoms than those aged over 45 years old (OR, 1.91, 95% CI, 1.3–2.81 [P = 0.001]). In conclusion, COVID-19 patients tended to have a high prevalence of adverse psychological events. Early identification and intervention should be conducted to avoid extreme events such as self-mutilating or suicidal impulsivity for

COVID-19 patients, especially for those with low education levels and females who have undergone divorce or bereavement.

Reference

https://www.nature.com/articles/s41398-021-01259-0

Integrated vaccination and physical distancing interventions to prevent future COVID-19 waves in Chinese cities

Abstract

The coronavirus disease 2019 (COVID-19) pandemic has posed substantial challenges to the formulation of preventive interventions, particularly since the effects of physical distancing measures and upcoming vaccines on reducing susceptible social contacts and eventually halting transmission remain unclear. Here, using anonymized mobile geolocation data in China, a mobility-associated social contact index was devised to quantify the impact of both physical distancing and vaccination measures in a unified way. Building on this index, our epidemiological model reveals that vaccination combined with physical distancing can contain resurgences without relying on stay-at-home restrictions, whereas a gradual vaccination process alone cannot achieve this. Further, for cities with medium population density, vaccination can reduce the duration of physical distancing by 36% to 78%, whereas for cities with high population density, infection numbers can be well-controlled through moderate physical distancing. These findings improve our understanding of the joint effects of vaccination and physical distancing with respect to a city's population density and social contact patterns.

Reference

https://www.nature.com/articles/s41562-021-01063-2

NEWSLETTER

Publication Date: Feb 24, 2021

Longer infections could fuel COVID variant's spread

Preliminary findings suggest that B.1.1.7, a SARS-CoV-2 variant first identified in the United Kingdom, might be more transmissible than earlier variants because it spends more time inside its host. Previous studies have estimated that B.1.1.7, which is now spreading rapidly in a number of countries, is roughly 50% more contagious than earlier coronavirus variants. Yonatan Grad at the Harvard T. H. Chan School of Public Health in Boston, Massachusetts, and his colleagues examined the results of daily SARS-CoV-2 tests on 65 people infected with the virus, including 7 infected with B.1.1.7. The team looked at how long the virus persisted, and the amount of virus present at each time point. In people with B.1.1.7, infections lasted an average of 13.3 days, compared with 8.2 days in those with other variants. These findings hint that B.1.1.7 is more easily transmitted than other variants because people who catch it are infected for longer, and can therefore pass the virus on to more contacts. This suggests that longer quarantine periods might be warranted for individuals infected with this variant. Fore more details, read the link given below.

Reference

https://www.nature.com/articles/d41586-021-00459-4

PERSPECTIVE

Publication Date: Feb 22, 2021

Autophagosome maturation stymied by SARS-CoV-2

Many pathogens are capable of disrupting autophagy within host cells. Miao *et al.* discover that the SARS-CoV-2 protein ORF3a inhibits autophagosome-lysosome fusion by dysregulating the HOPS complex.

Miao *et al.* then systematically tested the interactions between ORF3a and the collection of tethering factors and SNARE complexes coordinating autophagosome-lysosome fusion. They found that ORF3a consistently displayed a strong interaction with VPS39, a component of the HOPS complex, one of the tethering factors essential for autophagosome-lysosome fusion. ORF3a sequesters the HOPS complex (or part of the complex) to ORF3a-positive endosomes and lysosomes. Furthermore, the binding of ORF3a to VPS39 was shown to negatively impact HOPS complex assembly and even the formation of the STX17-SNAP29-VAMP8 SNARE complex that is essential for autophagosome-lysosome fusion. This ability to disrupt the fusion step of autophagy is unique to the ORF3a of SARS-CoV-2, as the highly similar ORF3a of SARS-CoV was found to be unable to interact with the HOPS complex and had no effect on autophagy. This difference in ORF3a function should be taken into account when explaining the difference in pathogenicity and infectivity of these two genetically similar viruses. For more details, read the link given below.

Reference

https://www.cell.com/developmental-cell/fulltext/S1534-5807(21)00113-1#fig1

PERSONAL VIEW

Publication Date: Feb 23, 2021

Scaling up COVID-19 rapid antigen tests: Promises and challenges

WHO recommends a minimum of 80% sensitivity and 97% specificity for antigen-detection rapid diagnostic tests (Ag-RDTs), which can be used for patients with symptoms consistent with COVID-19. However, after the acute phase when viral load decreases, use of Ag-RDTs might lead to high rates of false negatives, suggesting that the tests should be replaced by a combination of molecular and serological tests. When the likelihood of having COVID-19 is low, such as for asymptomatic individuals in low prevalence settings, for travel, return to schools, workplaces, and mass gatherings, Ag-RDTs with high negative predictive values can be used with confidence to rule out infection. For those who test positive in low prevalence settings, the high false positive rate means that mitigation strategies, such as molecular testing to confirm positive results, are needed. Ag-RDTs, when used appropriately, are promising tools for scaling up testing and ensuring that patient management and public health measures can be implemented without delay.

Reference

https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00048-7/fulltext

Publication Date: Feb 22, 2021

Importance of non-pharmaceutical interventions in lowering the viral inoculum to reduce susceptibility to infection by SARS-CoV-2 and potentially disease severity

Adherence to non-pharmaceutical interventions to prevent the transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been highly variable across settings, particularly in the USA. In this Personal View, data was reviewed supporting the importance of the viral inoculum (the dose of viral particles from an infected source over time) in increasing the probability of infection in respiratory, gastrointestinal, and sexually transmitted viral infections in humans. The available evidence was also reviewed, linking the relationship of the viral inoculum to disease

severity. Non-pharmaceutical interventions might reduce the susceptibility to SARS-CoV-2 infection by reducing the viral inoculum when there is exposure to an infectious source. Data from physical sciences research suggest that masks protect the wearer by filtering virus from external sources, and others by reducing expulsion of virus by the wearer. Social distancing, handwashing, and improved ventilation also reduce the exposure amount of viral particles from an infectious source. Maintaining and increasing non-pharmaceutical interventions can help to quell SARS-CoV-2 as we enter the second year of the pandemic. Finally, it was argued that even as safe and effective vaccines are being rolled out, non-pharmaceutical interventions will continue to play an essential role in suppressing SARS-CoV-2 transmission until equitable and widespread vaccine administration has been completed.

Reference

https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30982-8/fulltext

COMMENT

Publication Date: Feb 24, 2021

COVID-19 drug practices risk antimicrobial resistance evolution

Antimicrobial resistance is one of the biggest challenges facing modern medicine. Because the management of COVID-19 is increasingly becoming dependent on pharmacological interventions, there is greater risk for accelerating the evolution and spread of antimicrobial resistance. A study in a tertiary hospital environment revealed concerning colonisation patterns of microbes during extended periods. It also highlighted the diversity of antimicrobial resistance gene reservoirs in hospitals that could facilitate the emergence and transmission of new modes of antibiotic resistance. For more details, read the link given below.

Reference

https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247(21)00039-2/fulltext

Publication Date: Feb 23, 2021

SARS-CoV-2: Eye protection might be the missing key

Resistance emarkably, a year after the COVID-19 outbreak, ineffectual against widespread community infection was remained. Perhaps, something major is missing in our approach? The importance of aerosols versus droplets is debated—most viral transmission appears to be *via* virus-laden droplets, with the greatest risk in crowded, inadequately ventilated environments. Proximity to those infected poses the greatest risk. Currently, the presumed major viral invasion modalities involve inhalation or hand contamination of mucosal surfaces, despite studies to the contrary from a century ago showing the importance of eyes as an influenza infection route. Ocular surface droplet deposition is greatly underappreciated as a probable, frequent route for SARS-CoV-2 transmission.

Eye-protective face shields have been proposed to prevent community transmission. A large study showed that 19% of health-care workers became infected, despite wearing three-layered surgical masks, gloves, and shoe covers and using alcohol rub. After the

introduction of face shields, no worker was infected. For more details, read the link given below.

Reference

https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247(21)00040-9/fulltext

Anticipating outcomes for patients with COVID-19 and identifying prognosis patterns

Since its first description, SARS-CoV-2 has been the subject of more than 59 000 publications worldwide. Although SARS-CoV-2 infection mainly results in mild disease, during the first COVID-19 wave in France, up to 3% of patients required admission to hospital, 0·8% required intensive care unit admission, and overall mortality was reported to be around 0·5%. The ability to predict disease severity and subsequent course might help with triaging patients, optimising resource management, and understanding modifiable and non-modifiable factors involved in patient outcomes.

In *The Lancet Infectious Diseases*, Belén Gutiérrez-Gutiérrez and colleagues aimed to identify clinical phenotypes of COVID-19 among patients who required admission to hospital. In this large, multicentre, retrospective cohort study, the authors report the outcomes of 4035 patients with COVID-19 admitted to 127 Spanish hospitals between Feb 2 and March 17, 2020. The authors did a two-step cluster analysis to identify clinical characteristics associated with patient outcomes, and identified three phenotypes with adequate performance in predicting 30-day patient mortality in derivation, internal validation, and external validation cohorts. Ultimately, establishing whether these identified phenotypes could be helpful in clinical practice and how they could help us promote adequate management strategies in a rapidly changing epidemic will undoubtedly be the next important step. For more details, read the link given below.

Reference

https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00073-6/fulltext

SARS-CoV-2 infection and COVID-19 in asthmatics: A complex relationship

Risk of severe coronavirus disease 2019 (COVID-19) after infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is increased in patients with certain comorbidities, including chronic obstructive pulmonary disease (COPD). By contrast,

epidemiological data from many (but not all) countries indicate a low prevalence of asthma among patients with severe COVID-19. This reduced risk of severe COVID-19 may apply specifically to patients with the type 2 asthma endotype, which is most common in childhood asthma. For more details, read the link given below.

Reference

https://www.nature.com/articles/s41577-021-00516-z

Deadly COVID-19 among the elderly: Innate immune memory helping those most in need

Age is a key risk factor associated with the severity of symptoms caused by SARS-Co-V2 and there is an urgent need to reduce COVID-19 morbidity and mortality in elderly individuals. We discuss evidence suggesting that trained immunity elicited by BCG vaccination may improve immune responses and can serve as a strategy to combat COVID-19 in this population. For more details, read the link given below.

Reference

https://www.cell.com/med/fulltext/S2666-6340(21)00065-9

Publication Date: Feb 22, 2021

Vaccination against COVID-19: Expectations and concerns of patients with autoimmune and rheumatic diseases

Vaccination is an important and effective tool to prevent infections in the general population, as well as in patients with autoimmune and inflammatory rheumatic diseases. It has been well established that influenza and pneumococcal vaccination rates do not reach recommended levels in this target population, despite specific guidelines. Vaccine uptake has been negatively associated with low knowledge of vaccines and unfavorable attitudes towards vaccination in general. We did an international study (VAccinations against COVid-19 [VAXICOV]) to explore the feelings of patients and health-care professionals regarding COVID-19 vaccination. Our main objective was to describe the expectations and potential concerns related to COVID-19 vaccination of patients with systemic autoimmune or inflammatory rheumatic diseases and health-care professionals.

The study consisted of 57 web-based questions that addressed epidemiological, socio-demographic, and therapeutic elements associated with expectations and potential concerns regarding COVID-19 vaccination. The study targeted patients with a self-reported diagnosis of systemic autoimmune or inflammatory rheumatic diseases and health-care professionals. Health-care professionals were the control group and had no systemic autoimmune or inflammatory rheumatic diseases. Dissemination of the study was ensured through social media and mailings via patient associations and various medical societies (not only limited to rheumatologists) between Dec 12 and Dec 21, 2020. The study was approved by the ethics review board of Strasbourg (#CE-2020–199), and respondents gave their consent to participate to the study.

Data from the VAXICOV study are crucial to understand the main expectations and concerns regarding COVID-19 vaccination in patients with systemic autoimmune or inflammatory rheumatic diseases and health-care workers and to allow the identification of valuable strategies to increase vaccine coverage in those populations. For more details, read the link given below.

Reference

https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(21)00039-4/fulltext

CORRESPONDANCE

Publication Date: Feb 19, 2021

Risk and course of SARS-CoV-2 infection in patients treated for hypothyroidism and hyperthyroidism

COVID-19, caused by SARS-CoV-2, has spread dramatically, and by the end of January, 2021, had affected more than 100 million people, claiming more than 2.2 million lives. Older age, male sex, and the presence of comorbidities, such as hypertension, obesity, and diabetes have been identified as risk factors for severe disease and death. Patients with hypothyroidism or hyperthyroidism might have an increased risk of developing a severe course of COVID-19. First, because SARS-CoV-2 uses angiotensin-converting enzyme 2 (ACE2) as a receptor for host-cell entry, thyroid dysfunction might influence the risk and course of COVID-19 because the tissue distribution of ACE2 is influenced by serum concentrations of thyroid hormones. Second, patients with hypothyroidism and hyperthyroidism have an increased burden of cardiovascular and psychiatric comorbidities, which are also reported in patients with severe COVID-19. Third, the susceptibility to infection and course of infection might be negatively affected by thyroid dysfunction. Whether these pathophysiological observations in patients with thyroid disease translate into increased risk of acquiring or a worse prognosis of SARS-CoV-2 infection is unknown. Because hypothyroidism and hyperthyroidism are common conditions, any such increased risk would have an important public health impact. For more details, read the link given below.

Reference

https://www.thelancet.com/journals/landia/article/PIIS2213-8587(21)00028-0/fulltext

Publication Date: Feb 18, 2021

Early rate reductions of SARS-CoV-2 infection and COVID-19 in BNT162b2 vaccine recipients

In December, 2020, the Israeli Government approved the BNT162b2 COVID-19 vaccine and initiated a national immunisation campaign prioritising health-care workers (HCWs),

as in other countries. This campaign coincided with a third wave of COVID-19, peaking at 10 116 daily new cases by mid-January, 2021. The Sheba Medical Centre, Israel's largest hospital with 9647 HCWs, began staff vaccination on Dec 19, 2020. All HCWs, excluding those with previous SARS-CoV-2 infection, were eligible for vaccination. Clinical trial data of BNT162b2 vaccine estimated an early vaccine efficacy in preventing COVID-19 of 52·4% before dose two, and 90.5% on days 2–7 after dose two. A recent analysis of BNT162b2 vaccine data estimated vaccine efficacy of 89–91% during days 15–28 after the first dose. Early reductions in SARS-CoV-2 infection and COVID-19 rates in vaccinated HCWs were examined. For more details, read the link given below.

Reference

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00448-7/fulltext

REPORT

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SARS-CoV-2 Mpro inhibitors with antiviral activity in a transgenic mouse model

The COVID-19 pandemic caused by the SARS-CoV-2 virus continually poses serious threats to global public health. The main protease (M^{pro}) of SARS-CoV-2 plays a central role in viral replication. We designed and synthesized 32 new bicycloproline-containing Mpro inhibitors derived from either Boceprevir or Telaprevir, both of which are approved antivirals. All compounds inhibited SARS-CoV-2 M^{pro} activity *in vitro* with IC_{50} values ranging from 7.6 to 748.5 nM. The co-crystal structure of M^{pro} in complex with MI-23, one of the most potent compounds, revealed its interaction mode. Two compounds (MI-09 and MI-30) showed excellent antiviral activity in cell-based assays. In a SARS-CoV-2 infection transgenic mouse model, oral or intraperitoneal treatment with MI-09 or MI-30 significantly reduced lung viral loads and lung lesions. Both also displayed good pharmacokinetic properties and safety in rats. For more details, read the link given below.

Reference

https://science.sciencemag.org/content/early/2021/02/17/science.abf1611