

COVID-19

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RESEARCH PUBLICATIONS

Publication Date: Nov 11, 2020

A clade of SARS-CoV-2 viruses associated with lower viral loads in patient upper airways

Abstract

Background: The rapid spread of SARS-CoV-2, the causative agent of Coronavirus disease 2019 (COVID-19), has been accompanied by the emergence of distinct viral clades, though their clinical significance remains unclear. Here, we aimed to investigate the phylogenetic characteristics of SARS-CoV-2 infections in Chicago, Illinois, and assess their relationship to clinical parameters.

Methods: Whole-genome sequencing of SARS-CoV-2 isolates were performed, which were collected from COVID-19 patients in Chicago in mid-March, 2020. Using these and other publicly available sequences, we performed phylogenetic, phylogeographic, and phylodynamic analyses. Patient data was assessed for correlations between demographic or clinical characteristics and virologic features.

Findings: The 88 SARS-CoV-2 genome sequences in our study separated into three distinct phylogenetic clades. Clades 1 and 3 were most closely related to viral sequences from New York and Washington state, respectively, with relatively broad distributions across the US. Clade 2 was primarily found in the Chicago area with limited distribution elsewhere. At the time of diagnosis, patients infected with Clade 1 viruses had significantly higher average viral loads in their upper airways relative to patients infected with Clade 2 viruses, independent of disease severity.

Interpretation: These results show that multiple variants of SARS-CoV-2 were circulating in the Chicago area in mid-March 2020 that differed in their relative viral

loads in patient upper airways. These data suggest that differences in virus genotype can impact viral load and may influence viral spread.

Reference

[https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964\(20\)30488-6/fulltext](https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(20)30488-6/fulltext)

Cost-effectiveness of public health strategies for COVID-19 epidemic control in South Africa: A microsimulation modelling study

Abstract

Background: Health-care resource constraints in low-income and middle-income countries necessitate the identification of cost-effective public health interventions to address COVID-19. It was aimed to develop a dynamic COVID-19 microsimulation model to assess clinical and economic outcomes and cost-effectiveness of epidemic control strategies in KwaZulu-Natal province, South Africa.

Methods: Different combinations of five public health interventions: health-care testing alone were compared, where diagnostic testing is done only for individuals presenting to health-care centres; contact tracing in households of cases; isolation centres, for cases not requiring hospital admission; mass symptom screening and molecular testing for symptomatic individuals by community health-care workers; and quarantine centres, for household contacts who test negative. Infection transmission rates were calibrated to match effective reproduction number (R_e) estimates reported in South Africa. Two main epidemic scenarios were assessed for a period of 360 days, with an R_e of 1.5 and 1.2. Strategies with incremental cost-effectiveness ratio (ICER) of less than US\$3250 per year of life saved were considered cost-effective. Sensitivity analyses was also done by varying key parameters (R_e values, molecular testing sensitivity, and efficacies and costs of interventions) to determine the effect on clinical and cost projections.

Findings: When R_e was 1.5, health-care testing alone resulted in the highest number of COVID-19 deaths during the 360-day period. Compared with health-care testing alone, a combination of health-care testing, contact tracing, use of isolation centres, mass symptom screening, and use of quarantine centres reduced mortality by 94%, increased health-care costs by 33%, and was cost-effective (ICER \$340 per year of life saved). In

settings where quarantine centres were not feasible, a combination of health-care testing, contact tracing, use of isolation centres, and mass symptom screening was cost-effective compared with health-care testing alone (ICER \$590 per year of life saved). When R_e was 1.2, health-care testing, contact tracing, use of isolation centres, and use of quarantine centres was the least costly strategy, and no other strategies were cost-effective. In sensitivity analyses, a combination of health-care testing, contact tracing, use of isolation centres, mass symptom screening, and use of quarantine centres was generally cost-effective, with the exception of scenarios in which R_e was 2.6 and when efficacies of isolation centres and quarantine centres for transmission reduction were reduced.

Interpretation: In South Africa, strategies involving household contact tracing, isolation, mass symptom screening, and quarantining household contacts, who test negative would substantially reduce COVID-19 mortality and would be cost-effective. The optimal combination of interventions depends on epidemic growth characteristics and practical implementation considerations.

Reference

[https://www.thelancet.com/journals/langlo/article/PIIS2214-109X\(20\)30452-6/fulltext](https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(20)30452-6/fulltext)

Compositional cyber-physical epidemiology of COVID-19

Abstract

The COVID-19 pandemic has posed significant challenges globally. Countries have adopted different strategies with varying degrees of success. Epidemiologists are studying the impact of government actions using scenario analysis. However, the interactions between the government policy and the disease dynamics are not formally captured. For the first time, it was formally study the interaction between the disease dynamics, which is modelled as a physical process, and the government policy, which is modelled as the adjoining controller. The approach enables compositionality, where either the plant or the controller could be replaced by an alternative model. The work is inspired by the engineering approach for the design of Cyber-Physical Systems. Consequently, the new framework Compositional Cyber-Physical Epidemiology was termed. Different classes of controllers were created and applied these to control the

disease in New Zealand and Italy. Our controllers closely follow government decisions based on their published data. The pandemic progression was reproduced faithfully in New Zealand and Italy but also show the tradeoffs produced by differing control actions.

Reference

<https://www.nature.com/articles/s41598-020-76507-2>

SARS-CoV-2 receptor is co-expressed with elements of the kinin–kallikrein, renin–angiotensin and coagulation systems in alveolar cells

Abstract

SARS-CoV-2, the pathogenic agent of COVID-19, employs angiotensin converting enzyme-2 (ACE2) as its cell entry receptor. Clinical data reveal that in severe COVID-19, SARS-CoV-2 infects the lung, leading to a frequently lethal triad of respiratory insufficiency, acute cardiovascular failure, and coagulopathy. Physiologically, ACE2 plays a role in the regulation of three systems that could potentially be involved in the pathogenesis of severe COVID-19: the kinin–kallikrein system, resulting in acute lung inflammatory edema; the renin–angiotensin system, promoting cardiovascular instability; and the coagulation system, leading to thromboembolism. Here we assembled a healthy human lung cell atlas meta-analysis with ~130,000 public single-cell transcriptomes and show that key elements of the bradykinin, angiotensin and coagulation systems are co-expressed with ACE2 in alveolar cells and associated with their differentiation dynamics, which could explain how changes in ACE2 promoted by SARS-CoV-2 cell entry result in the development of the three most severe clinical components of COVID-19.

Reference

<https://www.nature.com/articles/s41598-020-76488-2>

Modelling transmission and control of the COVID-19 pandemic in Australia

Abstract

There is a continuing debate on relative benefits of various mitigation and suppression strategies aimed to control the spread of COVID-19. Here we report the results of

agent-based modelling using a fine-grained computational simulation of the ongoing COVID-19 pandemic in Australia. This model is calibrated to match key characteristics of COVID-19 transmission. An important calibration outcome is the age-dependent fraction of symptomatic cases, with this fraction for children found to be one-fifth of such fraction for adults. We apply the model to compare several intervention strategies, including restrictions on international air travel, case isolation, home quarantine, social distancing with varying levels of compliance, and school closures. School closures are not found to bring decisive benefits unless coupled with high level of social distancing compliance. We report several trade-offs, and an important transition across the levels of social distancing compliance, in the range between 70% and 80% levels, with compliance at the 90% level found to control the disease within 13–14 weeks, when coupled with effective case isolation and international travel restrictions.

Reference

<https://www.nature.com/articles/s41467-020-19393-6>

Long-distance airborne dispersal of SARS-CoV-2 in COVID-19 wards

Abstract

Evidence suggests that SARS-CoV-2, as well as other coronaviruses, can be dispersed and potentially transmitted by aerosols directly or via ventilation systems. We therefore investigated ventilation openings in one COVID-19 ward and central ducts that expel indoor air from three COVID-19 wards at Uppsala University Hospital, Sweden, during April and May 2020. Swab samples were taken from individual ceiling ventilation openings and surfaces in central ducts. Samples were subsequently subjected to rRT-PCR targeting the N and E genes of SARS-CoV-2. Central ventilation HEPA filters, located several stories above the wards, were removed and portions analyzed in the same manner. In two subsequent samplings, SARS-CoV-2 N and E genes were detected in seven and four out of 19 room vents, respectively. Central ventilation HEPA exhaust filters from the ward were found positive for both genes in three samples. Corresponding filters from two other, adjacent COVID-19 wards were also found positive. Infective ability of the samples was assessed by inoculation of susceptible cell cultures but could not be determined in these experiments. Detection of SARS-CoV-2 in

central ventilation systems, distant from patient areas, indicate that virus can be transported long distances and that droplet transmission alone cannot reasonably explain this, especially considering the relatively low air change rates in these wards. Airborne transmission of SARS-CoV-2 must be taken into consideration for preventive measures.

Reference

<https://www.nature.com/articles/s41598-020-76442-2>

COVID-Net: A tailored deep convolutional neural network design for detection of COVID-19 cases from chest X-ray images

Abstract

The Coronavirus Disease 2019 (COVID-19) pandemic continues to have a devastating effect on the health and well-being of the global population. A critical step in the fight against COVID-19 is effective screening of infected patients, with one of the key screening approaches being radiology examination using chest radiography. It was found in early studies that patients present abnormalities in chest radiography images that are characteristic of those infected with COVID-19. Motivated by this and inspired by the open source efforts of the research community, in this study we introduce COVID-Net, a deep convolutional neural network design tailored for the detection of COVID-19 cases from chest X-ray (CXR) images that is open source and available to the general public. To the best of the authors' knowledge, COVID-Net is one of the first open source network designs for COVID-19 detection from CXR images at the time of initial release. We also introduce COVIDx, an open access benchmark dataset that we generated comprising of 13,975 CXR images across 13,870 patient cases, with the largest number of publicly available COVID-19 positive cases to the best of the authors' knowledge. Furthermore, it was investigated how COVID-Net makes predictions using an explainability method in an attempt to not only gain deeper insights into critical factors associated with COVID cases, which can aid clinicians in improved screening, but also audit COVID-Net in a responsible and transparent manner to validate that it is making decisions based on relevant information from the CXR images. By no means a production-ready solution, the hope is that the open access COVID-Net,

along with the description on constructing the open source COVIDx dataset, will be leveraged and build upon by both researchers and citizen data scientists alike to accelerate the development of highly accurate yet practical deep learning solutions for detecting COVID-19 cases and accelerate treatment of those who need it the most.

Reference

<https://www.nature.com/articles/s41598-020-76550-z>

Structure and drug binding of the SARS-CoV-2 envelope protein transmembrane domain in lipid bilayers

Abstract

An essential protein of the SARS-CoV-2 virus, the envelope protein E, forms a homopentameric cation channel that is important for virus pathogenicity. Here it was reported a 2.1-Å structure and the drug-binding site of E's transmembrane domain (ETM), determined using solid-state NMR spectroscopy. In lipid bilayers that mimic the endoplasmic reticulum–Golgi intermediate compartment (ERGIC) membrane, ETM forms a five-helix bundle surrounding a narrow pore. The protein deviates from the ideal α -helical geometry due to three phenylalanine residues, which stack within each helix and between helices. Together with valine and leucine interdigitation, these cause a dehydrated pore compared with the viroporins of influenza viruses and HIV. Hexamethylene amiloride binds the polar amino-terminal lumen, whereas acidic pH affects the carboxy-terminal conformation. Thus, the N- and C-terminal halves of this bipartite channel may interact with other viral and host proteins semi-independently. The structure sets the stage for designing E inhibitors as antiviral drugs.

Reference

<https://www.nature.com/articles/s41594-020-00536-8>

Immune responses to SARS-CoV-2 in three children of parents with symptomatic COVID-19

Abstract

Compared to adults, children with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have predominantly mild or asymptomatic infections, but the underlying immunological differences remain unclear. Here, we describe clinical features, virology, longitudinal cellular, and cytokine immune profile, SARS-CoV-2-specific serology and salivary antibody responses in a family of two parents with PCR-confirmed symptomatic SARS-CoV-2 infection and their three children, who tested repeatedly SARS-CoV-2 PCR negative. Cellular immune profiles and cytokine responses of all children are similar to their parents at all timepoints. All family members have salivary anti-SARS-CoV-2 antibodies detected, predominantly IgA, that coincide with symptom resolution in 3 of 4 symptomatic members. Plasma from both parents and one child have IgG antibody against the S1 protein and virus-neutralizing activity detected. Using a systems serology approach, we demonstrate higher levels of SARS-CoV-2-specific antibody features of these family members compared to healthy controls. These data indicate that children can mount an immune response to SARS-CoV-2 without virological confirmation of infection, raising the possibility that immunity in children can prevent the establishment of SARS-CoV-2 infection. Relying on routine virological and serological testing may not identify exposed children, with implications for epidemiological and clinical studies across the life-span.

Reference

<https://www.nature.com/articles/s41467-020-19545-8>

Initial whole-genome sequencing and analysis of the host genetic contribution to COVID-19 severity and susceptibility

Abstract

The COVID-19 pandemic has accounted for millions of infections and hundreds of thousand deaths worldwide in a short-time period. The patients demonstrate a great diversity in clinical and laboratory manifestations and disease severity. Nonetheless, little is known about the host genetic contribution to the observed interindividual phenotypic variability. Here, the first host genetic study was reported in the Chinese population by deeply sequencing and analyzing 332 COVID-19 patients categorized by varying levels of severity from the Shenzhen Third People's Hospital. Upon a total of 22.2 million genetic variants, we conducted both single-variant and gene-based association tests among five severity groups including asymptomatic, mild, moderate, severe, and critical ill patients after the correction of potential confounding factors. Pedigree analysis suggested a potential monogenic effect of loss of function variants in GOLGA3 and DPP7 for critically ill and asymptomatic disease demonstration. Genome-wide association study suggests the most significant gene locus associated with severity were located in TMEM189–UBE2V1 that involved in the IL-1 signaling pathway. The p.Val197Met missense variant that affects the stability of the Tmprss2 protein displays a decreasing allele frequency among the severe patients compared to the mild and the general population. It was identified that the HLA-A*11:01, B*51:01, and C*14:02 alleles significantly predispose the worst outcome of the patients. This initial genomic study of Chinese patients provides genetic insights into the phenotypic difference among the COVID-19 patient groups and highlighted genes and variants that may help guide targeted efforts in containing the outbreak. Limitations and advantages of the study were also reviewed to guide future international efforts on elucidating the genetic architecture of host–pathogen interaction for COVID-19 and other infectious and complex diseases.

Reference

<https://www.nature.com/articles/s41421-020-00231-4>

Mobility network models of COVID-19 explain inequities and inform reopening

Abstract

The COVID-19 pandemic dramatically changed human mobility patterns, necessitating epidemiological models which capture the effects of changes in mobility on virus spread¹. It was introduced a metapopulation SEIR model that integrates fine-grained, dynamic mobility networks to simulate the spread of SARS-CoV-2 in 10 of the largest US metropolitan statistical areas. Derived from cell phone data, the mobility networks map the hourly movements of 98 million people from neighborhoods (census block groups, or CBGs) to points of interest (POIs) such as restaurants and religious establishments, connecting 57k CBGs to 553k POIs with 5.4 billion hourly edges. We show that by integrating these networks, a relatively simple SEIR model can accurately fit the real case trajectory, despite substantial changes in population behavior over time. Our model predicts that a small minority of “superspreader” POIs account for a large majority of infections and that restricting maximum occupancy at each POI is more effective than uniformly reducing mobility. Our model also correctly predicts higher infection rates among disadvantaged racial and socioeconomic groups 2–8 solely from differences in mobility: we find that disadvantaged groups have not been able to reduce mobility as sharply, and that the POIs they visit are more crowded and therefore higher-risk. By capturing who is infected at which locations, our model supports detailed analyses that can inform more effective and equitable policy responses to COVID-19.

Reference

<https://www.nature.com/articles/s41586-020-2923-3>

Lung transcriptome of a COVID-19 patient and systems biology predictions suggest impaired surfactant production which may be druggable by surfactant therapy

Abstract

An incomplete understanding of the molecular mechanisms behind impairment of lung pathobiology by COVID-19 complicates its clinical management. In this study, the gene expression pattern of cells was analyzed obtained from biopsies of COVID-19-affected patient and compared to the effects observed in typical SARS-CoV-2 and SARS-CoV-infected cell-lines. It was then compared gene expression patterns of COVID-19-

affected lung tissues and SARS-CoV-2-infected cell-lines and mapped those to known lung-related molecular networks, including hypoxia induced responses, lung development, respiratory processes, cholesterol biosynthesis and surfactant metabolism; all of which are suspected to be downregulated following SARS-CoV-2 infection based on the observed symptomatic impairments. Network analyses suggest that SARS-CoV-2 infection might lead to acute lung injury in COVID-19 by affecting surfactant proteins and their regulators SPD, SPC, and TTF1 through NSP5 and NSP12; thrombosis regulators PLAT, and EGR1 by ORF8 and NSP12; and mitochondrial NDUFA10, NDUF5, and SAMM50 through NSP12. Furthermore, hypoxia response through HIF-1 signaling might also be targeted by SARS-CoV-2 proteins. Drug enrichment analysis of dysregulated genes has allowed us to propose novel therapies, including lung surfactants, respiratory stimulants, sargramostim, and oseltamivir. The study presents a distinct mechanism of probable virus induced lung damage apart from cytokine storm.

Reference

<https://www.nature.com/articles/s41598-020-76404-8>

Publication Date: Nov 09, 2020

Bidirectional associations between COVID-19 and psychiatric disorder: retrospective cohort studies of 62 354 COVID-19 cases in the USA

Abstract

Background: Adverse mental health consequences of COVID-19, including anxiety and depression, have been widely predicted but not yet accurately measured. There are a range of physical health risk factors for COVID-19, but it is not known if there are also psychiatric risk factors. In this electronic health record network cohort study using data from 69 million individuals, 62 354 of whom had a diagnosis of COVID-19, we assessed whether a diagnosis of COVID-19 (compared with other health events) was associated with increased rates of subsequent psychiatric diagnoses, and whether patients with a history of psychiatric illness are at a higher risk of being diagnosed with COVID-19.

Methods: It was used the TriNetX Analytics Network, a global federated network that captures anonymised data from electronic health records in 54 health-care organisations in the USA, totalling 69·8 million patients. TriNetX included 62 354 patients diagnosed with COVID-19 between Jan 20, and Aug 1, 2020. We created cohorts of patients who had been diagnosed with COVID-19 or a range of other health events. Propensity score matching was used to control for confounding by risk factors for COVID-19 and for severity of illness. The incidence of and hazard ratios (HRs) was measured for psychiatric disorders, dementia, and insomnia, during the first 14 to 90 days after a diagnosis of COVID-19.

Findings: In patients with no previous psychiatric history, a diagnosis of COVID-19 was associated with increased incidence of a first psychiatric diagnosis in the following 14 to 90 days compared with six other health events (HR 2·1, 95% CI 1·8–2·5 vs influenza; 1·7, 1·5–1·9 vs other respiratory tract infections; 1·6, 1·4–1·9 vs skin infection; 1·6, 1·3–1·9 vs cholelithiasis; 2·2, 1·9–2·6 vs urolithiasis, and 2·1, 1·9–2·5 vs fracture of a large bone; all $p < 0·0001$). The HR was greatest for anxiety disorders, insomnia, and dementia. We observed similar findings, although with smaller HRs, when relapses and new diagnoses were measured. The incidence of any psychiatric diagnosis in the 14 to 90 days after COVID-19 diagnosis was 18·1% (95% CI 17·6–18·6), including 5·8% (5·2–6·4) that were a first diagnosis. The incidence of a first diagnosis of dementia in the 14 to 90 days after COVID-19 diagnosis was 1·6% (95% CI 1·2–2·1) in people older than 65 years. A psychiatric diagnosis in the previous year was associated with a higher incidence of COVID-19 diagnosis (relative risk 1·65, 95% CI 1·59–1·71; $p < 0·0001$). This risk was independent of known physical health risk factors for COVID-19, but we cannot exclude possible residual confounding by socioeconomic factors.

Interpretation: Survivors of COVID-19 appear to be at increased risk of psychiatric sequelae, and a psychiatric diagnosis might be an independent risk factor for COVID-19. Although preliminary, our findings have implications for clinical services, and prospective cohort studies are warranted.

Reference

[https://www.thelancet.com/journals/lanpsy/article/PIIS2215-0366\(20\)30462-4/fulltext](https://www.thelancet.com/journals/lanpsy/article/PIIS2215-0366(20)30462-4/fulltext)

Characteristics and outcomes of neonatal SARS-CoV-2 infection in the UK: A prospective national cohort study using active surveillance

Abstract

Background: Babies differ from older children with regard to their exposure to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). However, data describing the effect of SARS-CoV-2 in this group are scarce, and guidance is variable. It was aimed to describe the incidence, characteristics, transmission, and outcomes of SARS-CoV-2 infection in neonates who received inpatient hospital care in the UK.

Methods: A prospective UK population-based cohort study of babies with confirmed SARS-CoV-2 infection in the first 28 days of life was carried out, who received inpatient care between March 1 and April 30, 2020. Infected babies were identified through active national surveillance via the British Paediatric Surveillance Unit, with linkage to national testing, paediatric intensive care audit, and obstetric surveillance data. Outcomes included incidence (per 10 000 livebirths) of confirmed SARS-CoV-2 infection and severe disease, proportions of babies with suspected vertically and nosocomially acquired infection, and clinical outcomes.

Findings: It was identified 66 babies with confirmed SARS-CoV-2 infection (incidence 5.6 [95% CI 4.3–7.1] per 10 000 livebirths), of whom 28 (42%) had severe neonatal SARS-CoV-2 infection (incidence 2.4 [1.6–3.4] per 10 000 livebirths). 16 (24%) of these babies were born preterm. 36 (55%) babies were from white ethnic groups (SARS-CoV-2 infection incidence 4.6 [3.2–6.4] per 10 000 livebirths), 14 (21%) were from Asian ethnic groups (15.2 [8.3–25.5] per 10 000 livebirths), eight (12%) were from Black ethnic groups (18.0 [7.8–35.5] per 10 000 livebirths), and seven (11%) were from mixed or other ethnic groups (5.6 [2.2–11.5] per 10 000 livebirths). 17 (26%) babies with confirmed infection were born to mothers with known perinatal SARS-CoV-2 infection, two (3%) were considered to have possible vertically acquired infection (SARS-CoV-2-positive sample within 12 h of birth where the mother was also positive). Eight (12%) babies had suspected nosocomially acquired infection. As of July 28, 2020, 58 (88%) babies had been discharged home, seven (11%) were still admitted, and one (2%) had died of a cause unrelated to SARS-CoV-2 infection.

Interpretation: Neonatal SARS-CoV-2 infection is uncommon in babies admitted to hospital. Infection with neonatal admission following birth to a mother with perinatal SARS-CoV-2 infection was unlikely, and possible vertical transmission rare, supporting international guidance to avoid separation of mother and baby. The high proportion of babies from Black, Asian, or minority ethnic groups requires investigation.

Reference

[https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642\(20\)30342-4/fulltext](https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642(20)30342-4/fulltext)

Barriers to distance learning during the COVID-19 outbreak: A qualitative review from parents' perspective

Abstract

Aims: The goal of this study was to review the content posted in available local Jordanian Facebook groups to explore the perceptions of parents regarding the challenges of distance learning faced by their children during the coronavirus outbreak in Jordan.

Method: The Facebook search engine was used to identify local Facebook groups. The search keywords included distance learning, parents, and Jordan. Several faculty professors reviewed the posts and discussion flow on distance learning posted in Facebook groups from March 15th to April 25th 2020.

Results: The study identified a total of 248 posts and threads which categorized thematically for further analysis. The selected threads and answers revealed four underlying themes: (1) personal barriers (2) technical barriers (3) logistical barriers and (4) financial barriers.

Conclusion: Overall, parents were not limited to their daily routines during the pandemic. They performed the responsibility of helping school in teaching students. Many parents faced many types of barriers in their endeavors to assist their children with distance learning during the pandemic.

Reference

[https://www.cell.com/heliyon/fulltext/S2405-8440\(20\)32325-2](https://www.cell.com/heliyon/fulltext/S2405-8440(20)32325-2)

Hydroxychloroquine inhibits the trained innate immune response to interferons

Abstract

Hydroxychloroquine is being investigated for a potential prophylactic effect in SARS-CoV-2 infection, but its mechanism of action is poorly understood. Circulating leukocytes from the blood of COVID-19 patients show increased responses to Toll-Like Receptor ligands, suggestive of innate immune reprogramming. By analyzing interferon responses of peripheral blood mononuclear cells from healthy donors conditioned with heat-killed *Candida* the trained innate immunity can be modeled in vitro. In this model hydroxychloroquine inhibits the responsiveness of these innate immune cells to virus-like stimuli and interferons. This is associated with suppression of histone 3 lysine 27 acetylation and histone 3 lysine 4 trimethylation of inflammation-related genes, changes in the cellular lipidome, and decreased expression of interferon-stimulated genes. Our findings indicate that hydroxychloroquine inhibits trained immunity in vitro, which may not be beneficial for the antiviral innate immune response to SARS-CoV-2 infection in patients.

Reference

[https://www.cell.com/cell-reports-medicine/fulltext/S2666-3791\(20\)30190-7](https://www.cell.com/cell-reports-medicine/fulltext/S2666-3791(20)30190-7)

Real-time, interactive website for US-county-level COVID-19 event risk assessment

Abstract

Large events and gatherings, particularly those taking place indoors, have been linked to multitransmission events that have accelerated the pandemic spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). To provide real-time, geolocalized risk information, we developed an interactive online dashboard that estimates the risk that at least one individual with SARS-CoV-2 is present in gatherings of different sizes in the United States. The website combines documented case reports at the county level with ascertainment bias information obtained *via* population-wide serological surveys to estimate real-time circulating, per-capita infection rates. These rates are

updated daily as a means to visualize the risk associated with gatherings, including county maps and state-level plots. The website provides data-driven information to help individuals and policy makers make prudent decisions (for example, increasing mask-wearing compliance and avoiding larger gatherings) that could help control the spread of SARS-CoV-2, particularly in hard-hit regions.

Reference

<https://www.nature.com/articles/s41562-020-01000-9>

COVID-19 treatments and pathogenesis including anosmia in K18-hACE2 mice

Abstract

The ongoing COVID-19 pandemic is associated with substantial morbidity and mortality. Although much has been learned in the first months of the pandemic, many features of COVID-19 pathogenesis remain to be determined. For example, anosmia is a common presentation and many patients with this finding show no or only minor respiratory signs. Studies in animals experimentally infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the cause of COVID-19, provide opportunities to study aspects of the disease not easily investigated in human patients. Although COVID-19 severity ranges from asymptomatic to lethal, most experimental infections provide insights into mild disease. Here, using K18-hACE2 mice that we originally developed for SARS studies, it was shown that infection with SARS-CoV-2 causes severe disease in the lung, and in some mice, the brain. Evidence of thrombosis and vasculitis was detected in mice with severe pneumonia. Furthermore, it was shown that infusion of convalescent plasma from a recovered patient with COVID-19 protected against lethal disease. Mice developed anosmia at early times after infection. Notably, although pre-treatment with convalescent plasma prevented notable clinical disease, it did not prevent anosmia. Thus, K18-hACE2 mice provide a useful model for studying the pathological underpinnings of both mild and lethal COVID-19 and for assessing therapeutic interventions.

Reference

<https://www.nature.com/articles/s41586-020-2943-z>

The outcomes of the postulated interaction between SARS-CoV-2 and the renin-angiotensin system on the clinician's attitudes toward hypertension treatment

Abstract

Concern has arisen about the role played in coronavirus disease 2019 (COVID-19) infection by angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs). This study was designed to assess the practice behaviors of physicians toward hypertension treatment with ACE-i or ARBs during the COVID-19 pandemic. A self-administered survey questionnaire consisting of 26 questions about current hypertension treatment with ACE-i/ ARBs was applied to cardiologists, internists, and family physicians in central and western Turkey, between 01 and 19 May 2020. A total of 460 physicians were approached, and 220 (47.8%) participated in the study. Of the total respondents, 78.7% reported that they had not changed their antihypertensive medication prescribing pattern, 8.6% of clinicians had changed ACE-i/ ARBs medicine of patients during the COVID-19 pandemic and 12.7% of them were undecided. The median (\pm interquartile range) score indicating general reliance level of physicians in ACE-i/ARBs therapy was 8 ± 4 (range, 1–10). In multiple comparison analyses, the general reliance level in ACE-i/ARBs, reliance level when starting a new ACEi/ARBs and changing behavior in heart failure patients were significantly different with regard to the specialties ($p:0.02$, $p:0.009$, $p:0.005$ respectively). Although most of the physicians found the publications about ACE-i/ ARBs during the COVID-19 pandemic untrustworthy, there were variable levels of knowledge and reliance among different physicians and specialty groups. In general, the ACE-i/ ARBs prescribing habits were not affected by safety concerns during the COVID-19 pandemic in Turkey.

Reference

<https://www.nature.com/articles/s41371-020-00436-w>

Proinflammatory IgG Fc structures in patients with severe COVID-19

Abstract

Severe acute respiratory syndrome coronavirus 2 infections can cause coronavirus disease 2019 (COVID-19), which manifests with a range of severities from mild illness to life-threatening pneumonia and multi-organ failure. Severe COVID-19 is

characterized by an inflammatory signature, including high levels of inflammatory cytokines, alveolar inflammatory infiltrates and vascular microthrombi. Here we show that patients with severe COVID-19 produced a unique serologic signature, including an increased likelihood of IgG1 with afucosylated Fc glycans. This Fc modification on severe acute respiratory syndrome coronavirus 2 IgGs enhanced interactions with the activating Fcγ receptor FcγR11a; when incorporated into immune complexes, Fc afucosylation enhanced production of inflammatory cytokines by monocytes, including interleukin-6 and tumor necrosis factor. These results show that disease severity in COVID-19 correlates with the presence of proinflammatory IgG Fc structures, including afucosylated IgG1.

Reference

<https://www.nature.com/articles/s41590-020-00828-7>

Publication Date: Nov 07, 2020

An efficient approach based on 3D reconstruction of CT scan to improve the management and monitoring of COVID-19 patients

Abstract

Purpose: To reconstruct a 3D visualization from CT images of COVID-19 patients in order to improve understanding of the disease for better management and follow-up.

Materials and methods: CT Images of 185 COVID-19 patients was retrieved from the Cheikh Zaid International University Hospital in Rabat, Morocco. We then performed computer processing that allowed us to obtain a 3D visualization of these patients.

Results: In this article, it was chosen to do 3D reconstruction of three specific cases among 185 patients:

- Cases (A1, A2) which are negative RT-PCR patient with normal CT images.
- Cases (B1, B2) which are positive RT-PCR patient with abnormal CT images.
- Case (C) which is a negative RT-PCR patient with CT abnormalities.

To improve our results and have a better quality of the 3D reconstruction, we used different algorithms and a specific row data processing.

Conclusion: 3D reconstruction has a significant role in the diagnosis and management of COVID-19 patients. The quality and reliability of 3D reconstructions allow the clinician to make a quick and efficient diagnosis and avoid an eventual false negative (produced by the RT-PCR test). We suggest including chest 3D reconstruction in the patient management and prognosis evaluation.

Reference

[https://www.cell.com/heliyon/fulltext/S2405-8440\(20\)32296-9](https://www.cell.com/heliyon/fulltext/S2405-8440(20)32296-9)

Publication Date: Nov 06, 2020

Survey on general awareness, mental state and academic difficulties among students due to COVID-19 outbreak in the western regions of Uganda

Abstract

This academic research is carried out to assess the general awareness, mental state and academic difficulties among different age groups of students studying in various schools, colleges, or Universities during this lockdown period due to the COVID-19 crisis in the western regions of Uganda. An aggregate of 405 students participated in this survey. Among them 253 students are from rural regions, 59 students are from semi-urban regions and 93 students are from urban regions. This survey is classified into three sections: the first section spotlights the perceptive level of students about the COVID-19 crisis, the second section emphasizes the mental state of students and the final section highlights the academic difficulties faced by the students during this lockdown period. A statistical run is deliberated with the aid of SPSS version 20 software to evaluate the significance level ($P\text{-Value} < 0.05$) of each question among the localities.

Reference

[https://www.cell.com/heliyon/fulltext/S2405-8440\(20\)32297-0](https://www.cell.com/heliyon/fulltext/S2405-8440(20)32297-0)

Mucus production stimulated by IFN-AhR signaling triggers hypoxia of COVID-19

Abstract

Silent hypoxia has emerged as a unique feature of coronavirus disease 2019 (COVID-19). In this study, it was shown that mucins are accumulated in the bronchoalveolar lavage fluid (BALF) of COVID-19 patients and are upregulated in the lungs of severe respiratory syndrome coronavirus 2 (SARS-CoV-2)-infected mice and macaques. We find that induction of either interferon (IFN)- β or IFN- γ upon SARS-CoV-2 infection results in activation of aryl hydrocarbon receptor (AhR) signaling through an IDO-Kyn-dependent pathway, leading to transcriptional upregulation of the expression of mucins, both the secreted and membrane-bound, in alveolar epithelial cells. Consequently, accumulated alveolar mucus affects the blood-gas barrier, thus inducing hypoxia and diminishing lung capacity, which can be reversed by blocking AhR activity. These findings potentially explain the silent hypoxia formation in COVID-19 patients, and suggest a possible intervention strategy by targeting the AhR pathway.

Reference

<https://www.nature.com/articles/s41422-020-00435-z>

Age-severity matched cytokine profiling reveals specific signatures in Covid-19 patients

Abstract

A global effort is currently undertaken to restrain the COVID-19 pandemic. Host immunity has come out as a determinant for COVID-19 clinical outcomes, and several studies investigated the immune profiling of SARS-CoV-2 infected people to properly direct the clinical management of the disease. Thus, lymphopenia, T-cell exhaustion, and the increased levels of inflammatory mediators have been described in COVID-19 patients, in particular in severe cases¹. Age represents a key factor in COVID-19 morbidity and mortality². Understanding age-associated immune signatures of patients are therefore important to identify preventive and therapeutic strategies. In this study, we investigated the immune profile of COVID-19 hospitalized patients identifying a distinctive age-dependent immune signature associated with disease severity. Indeed, defined circulating factors - CXCL8, IL-10, IL-15, IL-27, and TNF- α - positively correlate

with older age, longer hospitalization, and a more severe form of the disease and may thus represent the leading signature in critical COVID-19 patients.

Reference

<https://www.nature.com/articles/s41419-020-03151-z>

Publication Date: Nov 05, 2020

High prevalence of SARS-CoV-2 antibodies in care homes affected by COVID-19: Prospective cohort study, England

Abstract

Background: Six London care homes experiencing a COVID-19 outbreak were investigated and found high rates of SARS-CoV-2 infection among residents and staff. Here, follow-up investigations were reported including antibody testing in the same care homes five weeks later.

Methods: Residents and staff in the initial investigation had a repeat nasal swab for SARS-CoV-2 RT-PCR and a blood test for SARS CoV-2 antibodies using ELISA based on SARS-CoV-2 native viral antigens derived from infected cells and virus neutralisation.

Findings: Of the 518 residents and staff in the initial investigation, 186/241 (77.2%) surviving residents and 208/254 (81.9%) staff underwent serological testing. Almost all SARS-CoV-2 RT-PCR positive residents and staff were seropositive five weeks later, whether symptomatic (residents 35/35, 100%; staff, 22/22, 100%) or asymptomatic (residents 32/33, 97.0%; staff 21/22, 95.5%). Symptomatic but SARS-CoV-2 RT-PCR negative residents and staff also had high seropositivity rates (residents 23/27, 85.2%; staff 18/21, 85.7%), as did asymptomatic RT-PCR negative individuals (residents 61/91, 67.0%; staff 95/143, 66.4%). Neutralising antibody was detected in 118/132 (89.4%) seropositive individuals and was not associated with age or symptoms. Ten residents (10/79 re-tested, 12.7%) remained RT-PCR positive but with higher RT-PCR cycle threshold values; 7/10 had serological testing and all were seropositive. New infections were detected in three residents and one staff.

Interpretation: RT-PCR provides a point prevalence of SARS-CoV-2 infection but significantly underestimates total exposure in outbreak settings. In care homes experiencing large COVID-19 outbreaks, most residents and staff had neutralising SARS-CoV-2 antibodies, which was not associated with age or symptoms.

Reference

[https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370\(20\)30341-2/fulltext](https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(20)30341-2/fulltext)

Effect of pre-exposure use of hydroxychloroquine on COVID-19 mortality: a population-based cohort study in patients with rheumatoid arthritis or systemic lupus erythematosus using the OpenSAFELY platform

Abstract

Background: Hydroxychloroquine has been shown to inhibit entry of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) into epithelial cells *in vitro*, but clinical studies found no evidence of reduced mortality when treating patients with COVID-19. It was aimed to evaluate the effectiveness of hydroxychloroquine for prevention of COVID-19 mortality, as opposed to treatment for the disease.

Methods: A prespecified observational, population-based cohort study was done using national primary care data and linked death registrations in the OpenSAFELY platform, which covers approximately 40% of the general population in England, UK. We included all adults aged 18 years and older registered with a general practice for 1 year or more on March 1, 2020. Cox regression was used to estimate the association between ongoing routine hydroxychloroquine use before the COVID-19 outbreak in England (considered as March 1, 2020) compared with non-users of hydroxychloroquine and risk of COVID-19 mortality among people with rheumatoid arthritis or systemic lupus erythematosus. Model adjustment was informed by a directed acyclic graph.

Findings: Between Sept 1, 2019, and March 1, 2020, of 194 637 people with rheumatoid arthritis or systemic lupus erythematosus, 30 569 (15·7%) received two or more prescriptions of hydroxychloroquine. Between March 1 and July 13, 2020, there were 547 COVID-19 deaths, 70 among hydroxychloroquine users. Estimated standardised cumulative COVID-19 mortality was 0·23% (95% CI 0·18 to 0·29) among users and

0.22% (0.20 to 0.25) among non-users; an absolute difference of 0.008% (-0.051 to 0.066). After accounting for age, sex, ethnicity, use of other immunosuppressive drugs, and geographical region, no association with COVID-19 mortality was observed (HR 1.03, 95% CI 0.80 to 1.33). No evidence of interactions was found with age or other immunosuppressive drugs. Quantitative bias analyses indicated that our observed associations were robust to missing information for additional biologic treatments for rheumatological disease. Similar associations was observed with the negative control outcome of non-COVID-19 mortality.

Interpretation: No evidence of a difference in COVID-19 mortality among people was found, who received hydroxychloroquine for treatment of rheumatological disease before the COVID-19 outbreak in England. Therefore, completion of randomised trials investigating pre-exposure prophylactic use of hydroxychloroquine for prevention of severe outcomes from COVID-19 are warranted.

Reference

[https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913\(20\)30378-7/fulltext](https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(20)30378-7/fulltext)

The short- and long-range RNA-RNA Interactome of SARS-CoV-2

Abstract

The Coronaviridae is a family of positive-strand RNA viruses that includes SARS-CoV-2, the etiologic agent of the COVID-19 pandemic. Bearing the largest single-stranded RNA genomes in nature, coronaviruses are critically dependent on long-distance RNA-RNA interactions to regulate the viral transcription and replication pathways. Here we experimentally mapped the in vivo RNA-RNA interactome of the full-length SARS-CoV-2 genome and subgenomic mRNAs. It was uncovered a network of RNA-RNA interactions spanning tens of thousands of nucleotides. These interactions reveal that the viral genome and subgenomes adopt alternative topologies inside cells, and engage in different interactions with host RNAs. Notably, we discovered a long-range RNA-RNA interaction - the FSE-arch - that encircles the programmed ribosomal frameshifting element. The FSE-arch is conserved in the related MERS-CoV and is under purifying selection. Our findings illuminate RNA structure based mechanisms governing

replication, discontinuous transcription, and translation of coronaviruses, and will aid future efforts to develop antiviral strategies.

Reference

[https://www.cell.com/molecular-cell/fulltext/S1097-2765\(20\)30782-6](https://www.cell.com/molecular-cell/fulltext/S1097-2765(20)30782-6)

New putative animal reservoirs of SARS-CoV-2 in Italian fauna: A bioinformatic approach

Abstract

SARS-CoV-2 is a virus belonging to the betacoronavirus family, causing fatal respiratory disease in humans, which became pandemic in 2020. Italy is one of the most affected countries by COVID-19, particularly in the northern regions. Several studies consider COVID-19 a zoonotic disease and, since Italy is the repository of a high biodiversity, SARS-CoV-2 infection in animals can be considered as a reservoir of the virus or favor the spreading between animals and humans. In this work, we analyzed the amino acid sequences of ACE2 protein of the most common domestic and wild animals present in Italy. Among the latter, we focused on ACE2 of the Chiroptera species present in Italy to identify the primary reservoir in this region. First, we reproduced in silico the Chiroptera ACE2/viral spike (S) protein interactions on the human ACE2/SARS-CoV-2 S complex model and identified the critical residues for the binding. In silico molecular docking of ACE2 belonging to Chiroptera vs SARS-CoV-2 S protein pointed to *Rhinolophus ferrumequinum* as a bat living in Italy, that may be a potential primary reservoir of the virus. On the other hand, a sequence similarity search on ACE2 of domestic and wild animals living in Italy pointed to domestic (horses, cats, cattle and sheep) and wild (European rabbits and grizzly bears) animal species as potential SARS-CoV-2 secondary reservoirs. Molecular docking of ACE2 belonging to these species vs S protein of Bat coronavirus (Bt-CoV/Rp3/2004) suggests that the primary reservoir *Rhinolophus ferrumequinum* may infect the secondary reservoirs, domestic and worldwide animals living in Italy, determining a specific risk of SARS-CoV-2 infection.

Reference

[https://www.cell.com/heliyon/fulltext/S2405-8440\(20\)32273-8](https://www.cell.com/heliyon/fulltext/S2405-8440(20)32273-8)

Effective screening of SARS-CoV-2 neutralizing antibodies in patient serum using lentivirus particles pseudotyped with SARS-CoV-2 spike glycoprotein

Abstract

Pseudotyped particles have significant importance and use in virology as tools for studying the biology of highly pathogenic viruses in a lower biosafety environment. The biological, chemical, and serological studies of the recently emerged SARS-CoV-2 will be greatly aided by the development and optimization of a suitable pseudotyping system. Here, we pseudotyped the SARS-CoV-2 Spike glycoprotein (SPG) on a traditional retroviral (MMLV) as well as a third generation lentiviral (pLV) vector and tested the transduction efficiency in several mammalian cell lines expressing SARS-CoV-2 receptor hACE2. While MMLV pseudotyped the vesicular stomatitis virus G glycoprotein (VSV-G) efficiently, it could not pseudotype the full-length SPG. In contrast, pLV pseudotyped both glycoproteins efficiently; however, much higher titers of pLV-G particles were produced. Among all the tested mammalian cells, 293Ts expressing hACE2 were most efficiently transduced using the pLV-S system. The pLV-S particles were efficiently neutralized by diluted serum (>:640) from recently recovered COVID-19 patients who showed high SARS-CoV-2 specific IgM and IgG levels. In summary, pLV-S pseudotyped virus provides a valid screening tool for the presence of anti SARS-CoV-2 specific neutralizing antibodies in convalescent patient serum.

Reference

<https://www.nature.com/articles/s41598-020-76135-w>

Cardiac adverse events associated with chloroquine and hydroxychloroquine exposure in 20 years of drug safety surveillance reports

Abstract

Chloroquine (CQ) and hydroxychloroquine (HCQ) are on the World Health Organization's List of Essential Medications for treating non-resistant malaria, rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). In addition, both drugs are currently used off-label in hospitals worldwide and in numerous clinical trials for the treatment of SARS-CoV-2 infection. However, CQ and HCQ use has been associated with cardiac side effects, which is of concern due to the higher risk of

COVID-19 complications in patients with heart related disorders, and increased mortality associated with COVID-19 cardiac complications. In this study we analyzed over thirteen million adverse event reports from the United States Food and Drug Administration Adverse Event Reporting System to confirm and quantify the association of cardiac side effects of CQ and HCQ. Additionally, we identified several confounding factors, including male sex, NSAID coadministration, advanced age, and prior diagnoses contributing to drug related cardiotoxicity. These findings may help guide therapeutic decision making and ethical trial design for COVID-19 treatment.

Reference

<https://www.nature.com/articles/s41598-020-76258-0>

Impact of tocilizumab administration on mortality in severe COVID-19

Abstract

The novel coronavirus disease 2019 (COVID-19) worldwide pandemic has placed a significant burden on hospitals and healthcare providers. The immune response to this disease is thought to lead to an aberrant inflammatory response or cytokine storm, which contributes to the severity of illness. There is an urgent need to confirm whether the use of tocilizumab provides a benefit in individuals with COVID-19. A single-center propensity-score matched cohort study, including all consecutive COVID-19 patients, admitted to the medical center who were either discharged from the medical center or expired between March 1, 2020, and May 5, 2020, was performed. Patients were stratified according to the receipt of tocilizumab for cytokine storm and matched to controls using propensity scores. The primary outcome was in-hospital mortality. A total of 274 patients meeting inclusion and exclusion criteria were identified and 132 patients were included in the matched dataset (tocilizumab = 66; no tocilizumab = 66). Approximately 73% of the patients were male. Hypertension (55%), diabetes mellitus (31%), and chronic pulmonary disease (15%) were the most common comorbidities present. There were 18 deaths (27.3%) in the tocilizumab group and 18 deaths (27.3%) in the no tocilizumab group (odds ratio, 1.0; 95% confidence interval, 0.465 – 2.151; $p = 1.00$). Advanced age, history of myocardial infarction, dementia, chronic pulmonary disease, heart failure, and malignancy were significantly more common in patients who

died. The current analysis does not support the use of tocilizumab for the management of cytokine storm in patients with COVID-19. Use of this therapeutic agent should be limited to the context of a clinical trial until more evidence is available.

Reference

<https://www.nature.com/articles/s41598-020-76187-y>

Searching for target-specific and multi-targeting organics for Covid-19 in the Drugbank database with a double scoring approach

Abstract

The current outbreak of Covid-19 infection due to SARS-CoV-2, a virus from the coronavirus family, has become a major threat to human healthcare. The virus has already infected more than 44 M people and the number of deaths reported has reached more than 1.1 M which may be attributed to lack of medicine. The traditional drug discovery approach involves many years of rigorous research and development and demands for a huge investment which cannot be adopted for the ongoing pandemic infection. Rather we need a swift and cost-effective approach to inhibit and control the viral infection. With the help of computational screening approaches and by choosing appropriate chemical space, it is possible to identify lead drug-like compounds for Covid-19. In this study, we have used the Drugbank database to screen compounds against the most important viral targets namely 3C-like protease (3CLpro), papain-like protease (PLpro), RNA-dependent RNA polymerase (RdRp) and the spike (S) protein. These targets play a major role in the replication/transcription and host cell recognition, therefore, are vital for the viral reproduction and spread of infection. As the structure based computational screening approaches are more reliable, we used the crystal structures for 3C-like main protease and spike protein. For the remaining targets, we used the structures based on homology modeling. Further, we employed two scoring methods based on binding free energies implemented in AutoDock Vina and molecular mechanics—generalized Born surface area approach. Based on these results, we propose drug cocktails active against the three viral targets namely 3CLpro, PLpro and RdRp. Interestingly, one of the identified compounds in this study i.e. Baloxavir marboxil has been under clinical trial for the treatment of Covid-19 infection. In addition, we have identified a few compounds such as Phthalocyanine, Tadalafil, Lonafarnib, Nilotinib,

Dihydroergotamine, R-428 which can bind to all three targets simultaneously and can serve as multi-targeting drugs. The study also included calculation of binding energies for various compounds currently under drug trials. Among these compounds, it is found that Remdesivir binds to targets, 3CLpro and RdRp with high binding affinity. Moreover, Baricitinib and Umifenovir were found to have superior target-specific binding while Darunavir is found to be a potential multi-targeting drug. As far as we know this is the first study where the compounds from the Drugbank database are screened against four vital targets of SARS-CoV-2 and illustrates that the computational screening using a double scoring approach can yield potential drug-like compounds against Covid-19 infection.

Reference

<https://www.nature.com/articles/s41598-020-75762-7>

[Deep learning-based model for detecting 2019 novel coronavirus pneumonia on high-resolution computed tomography](#)

Abstract

Computed tomography (CT) is the preferred imaging method for diagnosing 2019 novel coronavirus (COVID19) pneumonia. We aimed to construct a system based on deep learning for detecting COVID-19 pneumonia on high resolution CT. For model development and validation, 46,096 anonymous images from 106 admitted patients, including 51 patients of laboratory confirmed COVID-19 pneumonia and 55 control patients of other diseases in Renmin Hospital of Wuhan University were retrospectively collected. Twenty-seven prospective consecutive patients in Renmin Hospital of Wuhan University were collected to evaluate the efficiency of radiologists against 2019-CoV pneumonia with that of the model. An external test was conducted in Qianjiang Central Hospital to estimate the system's robustness. The model achieved a per-patient accuracy of 95.24% and a per-image accuracy of 98.85% in internal retrospective dataset. For 27 internal prospective patients, the system achieved a comparable performance to that of expert radiologist. In external dataset, it achieved an accuracy of 96%. With the assistance of the model, the reading time of radiologists was greatly decreased by 65%. The deep learning model showed a comparable performance with expert radiologist, and greatly improved the efficiency of radiologists in clinical practice.

Reference

<https://www.nature.com/articles/s41598-020-76282-0>

Distinct antibody responses to SARS-CoV-2 in children and adults across the COVID-19 clinical spectrum

Abstract

Clinical manifestations of COVID-19 caused by the new coronavirus SARS-CoV-2 are associated with age. Adults develop respiratory symptoms, which can progress to acute respiratory distress syndrome (ARDS) in the most severe form, while children are largely spared from respiratory illness but can develop a life-threatening multisystem inflammatory syndrome (MIS-C). Here, we show distinct antibody responses in children and adults after SARS-CoV-2 infection. Adult COVID-19 cohorts had anti-spike (S) IgG, IgM and IgA antibodies, as well as anti-nucleocapsid (N) IgG antibody, while children with and without MIS-C had reduced breadth of anti-SARS-CoV-2-specific antibodies, predominantly generating IgG antibodies specific for the S protein but not the N protein. Moreover, children with and without MIS-C had reduced neutralizing activity as compared to both adult COVID-19 cohorts, indicating a reduced protective serological response. These results suggest a distinct infection course and immune response in children independent of whether they develop MIS-C, with implications for developing age-targeted strategies for testing and protecting the population.

Reference

<https://www.nature.com/articles/s41590-020-00826-9>

PERSPECTIVE

Publication Date: Nov 06, 2020

The challenge and response of mental health institutions in COVID-19 pandemic: From chaos to new normal

Coronavirus disease 2019 (COVID-19) shows a global outbreak. Patients with mental disorders are categorized as a vulnerable group that faces a high risk of the disease. COVID-19 has a heavy impact on mental health. Mental health institutions in China, the first country to report COVID-19, have encountered unprecedented difficulties and challenges. In this article, we provide a brief summary of the challenges and lessons learned by first-line mental health staff in mental health institutions in China during this period, and we propose suggestions to deal with similar challenges in the future. For more details, read the link given below.

Reference

<https://www.nature.com/articles/s41398-020-01059-y>

COMMENT

Publication Date: Nov 11, 2020

Leveraging the COVID-19 response to end preventable child deaths from pneumonia

Pneumonia kills people, young and old. The world has been reminded of the toll of pneumonia as countries struggle to control the COVID-19 pandemic. COVID-19 has claimed more than 1 million lives so far in 2020, but other infectious diseases have caused pneumonia-related mortality for decades. Although there has been a commendable 54% decline in pneumonia-related deaths among children younger than 5 years since 2000, pneumonia is still the leading infectious cause of child deaths and claims more than 800 000 children's lives every year (WHO Maternal and Child Epidemiology Estimation, unpublished).

Although most children have less illness related to COVID-19 than adults, the potential secondary impacts of the pandemic could cause a reversal in progress in child survival. Robertson and colleagues used a model to estimate that, depending on the degree of severity, service disruptions, reductions in access to care because of lockdown measures, and increased rates of wasting due to food shortages over 12 months could cause between 506 900 and 2 313 900 additional deaths among children younger than 5 years. The data suggest that about a third of these preventable deaths could be from pneumonia and newborn sepsis. Review of routine health information and programme data across several countries indicate that since the onset of the pandemic there have been reductions in the numbers of children who attend outpatient services and who receive correct diagnosis and treatment of illnesses and immunisation services (UNICEF and Save the Children, unpublished). Drops in coverage of the pertussis, *Haemophilus influenzae* type b, pneumococcal, and measles vaccines, which all offer protection against pneumonia, put millions of children at risk of severe and potentially fatal infections. For more details, read the link given below.

Reference

[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)32348-5/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32348-5/fulltext)

RNA 2'-O-methylation modification and its implication in COVID-19 immunity

The recent outbreak of a novel human coronavirus infection (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a serious threat to public health, which has currently led to more than 25 million confirmed cases and more than 800 thousand deaths in 216 countries according to the World Health Organization (www.who.int). The current development of novel therapeutic and prophylactic approaches to SARS-CoV-2 infection could be categorized into at least four different strategies such as; (1) broad-spectrum antiviral agents, (2) drugs targeting the proinflammatory cytokines, (3) inhibitors of host cell proteases that participate in the priming of the viral spike protein, and (4) therapeutics targeting the virus–host interface linking the viral spike protein to the angiotensin-converting enzyme 2 (ACE2) receptor in host cells. Despite significant insights into SARS-CoV-2 replication, and virus–host interactions, there is currently no approved medications or vaccines that can cure or prevent SARS-CoV-2 infection.

Coronaviruses are a group of enveloped positive-sensed RNA viruses that replicate in host cell cytoplasm through a large membrane associated RNA replication/transcription machinery comprising at least 16 virus-encoded non-structural proteins (NSP1 to NSP16). Of these, NSP16 as a viral 2'-O-methyltransferase (2'-O-MTase), which function with its co-factor NSP10 activator protein are essential for methylation of 5'-end RNA cap2. Recent identification of SARS-CoV-2 2'-O-MTase led to the possibility of utilizing this pathway to both attenuate SARS-CoV-2 infection and develop novel therapeutic treatment options (Fig. 1).

Viral epitranscriptomics is an emerging field, which refers to post-transcriptional modifications of RNA and plays an important role in the life cycles of different viruses including human coronavirus. 2'-O-methylation (2'OMe) is one of the most common modification in the viral RNA including SARS-CoV-2 RNA. This modification is functionally linked to all stages of RNA metabolism such as structure, stability and interactions, and plays a critical role in several biological processes such as modulating the replication of viruses and antiviral immune responses. Accumulating evidence indicate that 2'-O-methylation of viral RNA (2'OMe-RNA) plays an important role in

evasion of cellular innate immune responses in the host cells. Züst and colleagues recently demonstrated that 2'OMe of viral RNA contributed to evasion of the interferon (IFN)-mediated antiviral response, thereby promoting viral replication. Moreover, human coronavirus mutants lacking 2'-O-MTase activity induced increased expression of IFN. These findings suggest that 2-OMe-RNA modification provides a molecular signature for discrimination of self from non-self RNA. More recent studies demonstrated that SARS-CoV2 replicate in the cytoplasm and encode their own viral 2'-O-MTase, which catalyze the formation of cap structures at the 5'-end of SARS-CoV-2 RNA to impede degradation by 5' exoribonucleases, ensure efficient translation, and evade recognition by the host cell innate immune system. These studies also showed that SARS-CoV2 2'-O-MTase (NSP16 protein), which requires a cofactor NSP10 for its proper activity and the NSP10-NSP16 complex is highly conserved between SARS-CoV, MERS, and SARS-CoV-2. Interestingly, nonmethylated RNA in cytoplasm is prone to degradation and cannot be efficiently translated. Crucially, the lack of 2'-O-MTase activity results in a significant attenuation of SARS-CoV infection, by decreased viral replication in vivo models. Therefore, SARS-CoV2 2'-O-MTase represents a potential target for antiviral drug development and activate intrinsic cell immunity against SARS-CoV-2 infection. Sharma and colleagues also recently identified that the SARS-CoV-2 genome encodes for 2'-O-MTase using its protein sequence, which plays an important role in methylation of viral RNA for evading host immune system. Moreover, they modeled the structure of 2'-O-MTase using a comparative modeling approach and screened the food and drug administration (FDA) approved drugs include antivirals, alkaloids, cardiac glycosides, anticancer, and steroids against 2'-O-MTase. Encinar et al. also used a virtual screening approach of molecular docking of FDA approved investigational and experimental drugs to identify potential candidates that can be directed to the SARS-CoV-2 2'-O-MTase. Therefore, these findings suggested that these drugs may act as specific inhibitor for SARS-CoV2 2'-O-MTase. In conclusion, the SARS-CoV-2 genome encodes for 2'-O-MTase, which plays a key role in methylation of SARS-CoV-2 RNA for evading host immune system. Therefore, SARS-CoV2 2'-O-MTase represents a potential target for FDA-approved broad-spectrum antiviral drugs or new small molecule inhibitors development and activate intrinsic antiviral immunity against SARS-CoV-2 infection.

Reference

<https://www.nature.com/articles/s41420-020-00358-z>

Publication Date: Nov 05, 2020

Hydroxychloroquine in the prevention of COVID-19 mortality

COVID-19 has affected tens of millions of individuals across the globe and upended the lives of countless others. Despite advances in supportive care and treatment, mortality remains high, and prevention of infection continues to be crucial. Early on in the pandemic, hydroxychloroquine was suggested as a possible prevention method or treatment for COVID-19, given evidence of in-vitro inhibition of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), propelling this mainstay treatment of rheumatic diseases to prominence and controversy. However, multiple high-quality studies subsequently showed no benefit of hydroxychloroquine use as post-exposure prophylaxis or as a COVID-19 treatment. As enthusiasm for hydroxychloroquine as a treatment of SARS-CoV-2 infection rapidly declined, the possibility of the use of this medication to prevent COVID-19 remained, with multiple randomised clinical trials designed to address this possibility. Furthermore, with the spotlight shone on hydroxychloroquine with regards to COVID-19, patients with rheumatic diseases and their care providers have been highly interested as to whether this commonly used medication for systemic lupus erythematosus and rheumatoid arthritis could protect against adverse outcomes of COVID-19.

In *The Lancet Rheumatology*, Christopher Rentsch and colleagues address whether hydroxychloroquine use before SARS-CoV-2 infection could prevent mortality from COVID-19.⁶ They did a population-based cohort study using the OpenSAFELY platform, an electronic health records database capturing 40% of the population of England. They included 30 569 patients with systemic lupus erythematosus or rheumatoid arthritis who were already taking hydroxychloroquine in the 6 months before what was considered as the start of the pandemic in England and 164 068 patients with these rheumatic diseases who did not use hydroxychloroquine.⁶ Their primary outcome was COVID-19 mortality per death certificate data, and they used cause-specific cox regression models, adjusting for age, sex, ethnicity, geographical region, and other immunosuppressive drugs (ie, other conventional synthetic disease-modifying

rheumatic drugs [DMARDs] and oral corticosteroids). The study found no significant difference in standardised cumulative COVID-19 mortality associated with hydroxychloroquine use (0.23% among hydroxychloroquine users and 0.22% among non-users) with an adjusted hazard ratio of 1.03 (95% CI 0.80–1.33). The findings were similar in an extended analysis additionally adjusting for established or suspected risk factors for COVID-19 mortality. Additionally, no difference was seen in non-COVID-19 mortality associated with hydroxychloroquine use.

Reference

[https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913\(20\)30390-8/fulltext](https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(20)30390-8/fulltext)

NEWSLETTER

Publication Date: Nov 11, 2020

Russia announces positive COVID-vaccine results from controversial trial

Abstract

On 9 November, New York City-based drug company Pfizer put out a press release on positive interim results from a coronavirus vaccine phase III trial, which was the first to report on the final round of human testing. It was also the first compelling evidence that a vaccine can prevent COVID-19. After 2 days, the developers of a Russian vaccine called Sputnik V have been announced, also in a press release, which seems to be similarly effective at preventing the disease.

The Gamaleya National Center of Epidemiology and Microbiology in Moscow and the Russian Direct Investment Fund said that an interim analysis of 20 COVID-19 cases identified among trial participants has found that the vaccine was 92% effective. The analysis looked at more than 16,000 volunteers — who received either the vaccine or a placebo — 3 weeks after they had taken the first dose. The trial has enrolled a total of 40,000 participants, the release said. The low number of cases reported in the Sputnik V trial means that there is less certainty that the vaccine's true efficacy is above 90%, compared with the Pfizer and BioNTech analysis, said Stephen Evans, an epidemiologist at the London School of Hygiene and Tropical Medicine, in a statement to the UK Science Media Centre (SMC). For more details, read the link given below.

Reference

<https://www.nature.com/articles/d41586-020-03209-0>

Big data and simple models used to track the spread of COVID-19 in cities

Abstract

Behind the highly politicized disagreements over COVID-19 control measures lies a widely shared desire to return economic and social life to sustainable levels as soon and for as long as possible, while preserving health-care systems and minimizing severe illness and death. The main arguments are about the extent to which these goals are mutually reinforcing, and whether there is a trade-off between greater viral transmission and increased social and economic activity. The difficulty in identifying control measures that are both effective and minimally disruptive motivates the search for new approaches to modelling transmission. Given the limited data available from epidemiological studies on how interventions can curb infection, such models can provide an initial framework for evaluating hypothetical control measures and help to guide policy decisions.

Writing in *Nature*, Chang *et al.* present an innovative method that combines simple infectious-disease models with human-mobility data obtained from mobile-phone records. This data-rich model has enabled them to generate and, to some extent, test hypotheses on where the virus is transmitted, how racial and socio-economic disparities in COVID-19 infections arise, and how effective different types of control measure might be. For more details, read the link given below.

Reference

<https://www.nature.com/articles/d41586-020-02964-4>