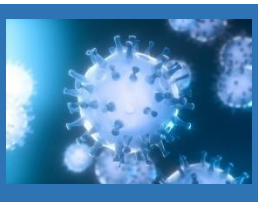
COVID-19

Dec 24 - 30, 2020



RESEARCH PUBLICATIONS

Publication Date: Dec 30, 2020

Fluid dynamics of COVID-19 airborne infection suggests urgent data for a scientific design of social distancing

Abstract

The COVID-19 pandemic is largely caused by airborne transmission, a phenomenon that rapidly gained the attention of the scientific community. Social distancing is of paramount importance to limit the spread of the disease, but to design social distancing rules on a scientific basis the process of dispersal of virus-containing respiratory droplets must be understood. Here, it is demonstrated that available knowledge is largely inadequate to make predictions on the reach of infectious droplets emitted during a cough and on their infectious potential. We follow the position and evaporation of thousands of respiratory droplets by massive state-of-the-art numerical simulations of the airflow caused by a typical cough. It was found that different initial distributions of droplet size taken from literature and different ambient relative humidity lead to opposite conclusions: (1) most versus none of the viral content settles in the first 1–2 m; (2) viruses are carried entirely on dry nuclei versus on liquid droplets; (3) small droplets travel less than 2.5m versus more than 7.5m. We point to two key issues that need to be addressed urgently in order to provide a scientific foundation to social distancing rules: (I1) a careful characterisation of the initial distribution of droplet sizes; (I2) the infectious potential of viruses carried on dry nuclei versus liquid droplets.

Reference

https://www.nature.com/articles/s41598-020-80078-7

Hydrogel particles improve detection of SARS-CoV-2 RNA from multiple sample types

Abstract

Here, a rapid and versatile method was presented for capturing and concentrating SARS-CoV-2 from contrived transport medium and saliva samples using affinity-capture magnetic hydrogel particles. It was demonstrated that the method concentrates virus from 1 mL samples prior to RNA extraction, substantially improving detection of virus using real-time RT-PCR across a range of viral titers (100–1,000,000 viral copies/mL) and enabling detection of virus using the 2019 nCoV CDC EUA Kit down to 100 viral copies/mL. This method is compatible with commercially available nucleic acid extraction kits (i.e., from Qiagen) and a simple heat and detergent method that extracts viral RNA directly off the particle, allowing a sample processing time of 10 min. We furthermore tested our method in transport medium diagnostic remnant samples that previously had been tested for SARS-CoV-2, showing that our method not only correctly identified all positive samples but also substantially improved detection of the virus in low viral load samples. The average improvement in cycle threshold value across all viral titers tested was 3.1. Finally, it was illustrated that the method could potentially be used to enable pooled testing, as we observed considerable improvement in the detection of SARS-CoV-2 RNA from sample volumes of up to 10 mL.

Reference

https://www.nature.com/articles/s41598-020-78771-8

State-specific projection of COVID-19 infection in the United States and evaluation of three major control measures

Abstract

Most models of the COVID-19 pandemic in the United States do not consider geographic variation and spatial interaction. In this research, we developed a travel-network-based susceptible-exposed-infectious-removed (SEIR) mathematical compartmental model system that characterizes infections by state and incorporates inflows and outflows of interstate travelers. Modeling reveals that curbing interstate travel when the disease is already widespread will make little difference. Meanwhile, increased testing capacity

(facilitating early identification of infected people and quick isolation) and strict social-distancing and self-quarantine rules are most effective in abating the outbreak. The modeling has also produced state-specific information. For example, for New York and Michigan, isolation of persons exposed to the virus needs to be imposed within 2 days to prevent a broad outbreak, whereas for other states this period can be 3.6 days. This model could be used to determine resources needed before safely lifting state policies on social distancing.

Reference

https://www.nature.com/articles/s41598-020-80044-3

Publication Date: Dec 29, 2020

Survival of the enveloped bacteriophage Phi6 (a surrogate for SARS-CoV-2) in evaporated saliva microdroplets deposited on glass surfaces

Abstract

Survival of respiratory viral pathogens in expelled saliva microdroplets is central to their transmission, yet the factors that determine survival in such microdroplets are not well understood. Here, microscopy imaging was combined with virus viability assays to study survival of three bacteriophages suggested as good models for respiratory pathogens: the enveloped Phi6 (a surrogate for SARS-CoV-2), and the non-enveloped PhiX174 and MS2. Virus viability was measured in human saliva microdroplets, SM buffer, and water following deposition on glass surfaces at various relative humidities (RH). Saliva and water microdroplets dried out rapidly, within minutes, at all tested RH levels (23%, 43%, 57%, and 78%), while SM microdroplets remained hydrated at RH ≥ 57%. Generally, the survival of all three viruses in dry saliva microdroplets was significantly greater than those in SM buffer and water under all RH (except PhiX174 in water under 57% RH survived the best among 3 media). Thus, atmosphere RH and microdroplet hydration state are not sufficient to explain virus survival, indicating that the virus-suspended medium, and association with saliva components in particular, likely play a role in virus survival. Uncovering the exact properties and components that make saliva a favorable environment for the survival of viruses, in particular enveloped ones like Phi6, is thus of

great importance for reducing transmission of viral respiratory pathogens including SARS-CoV-2.

Reference

https://www.nature.com/articles/s41598-020-79625-z

In-depth blood proteome profiling analysis revealed distinct functional characteristics of plasma proteins between severe and non-severe COVID-19 patients

Abstract

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has infected over forty million patients worldwide. Although most coronavirus disease 2019 (COVID-19) patients have a good prognosis, some develop severe illness. Markers that define disease severity or predict clinical outcome need to be urgently developed as the mortality rate in critical cases is approximately 61.5%. In the present study, we performed in-depth proteome profiling of undepleted plasma from eight COVID-19 patients. Quantitative proteomic analysis using the BoxCar method revealed that 91 out of 1222 quantified proteins were differentially expressed depending on the severity of COVID-19. Importantly, 76 proteins were found, previously not reported, which could be novel prognostic biomarker candidates. The proteome signatures captured the host response to SARS-CoV-2 infection, thereby highlighting the role of neutrophil activation, complement activation, platelet function, and T cell suppression as well as proinflammatory factors upstream and downstream of interleukin-6, interleukin-1B, and tumor necrosis factor. Consequently, this study supports the development of blood biomarkers and potential therapeutic targets to aid clinical decision-making and subsequently improve prognosis of COVID-19.

Reference

https://www.nature.com/articles/s41598-020-80120-8

ApoE isoform-dependent SARS-CoV-2 neurotropism and cellular response

Abstract

ApoE4, a strong genetic risk factor for Alzheimer's disease, has been associated with increased risk for severe COVID-19. However, it is unclear whether ApoE4 alters COVID-19 susceptibility or severity and the role of direct viral infection in brain cells remains obscure. The neurotropism of SARS-CoV2 was tested in human induced pluripotent stem cell (hiPSC) models and observed low-grade infection of neurons and astrocytes that is boosted in neuron-astrocyte co-cultures and organoids. Isogenic ApoE3/3 and ApoE4/4 hiPSCs were generated and found an increased rate of SARS-CoV-2 infection in ApoE4/4 neurons and astrocytes. ApoE4 astrocytes exhibited enlarged size and elevated nuclear fragmentation upon SARS-CoV-2 infection. Finally, it was shown that remdesivir treatment prevents SARS-CoV2 infection of hiPSC-neurons and astrocytes. These findings suggest that ApoE4 may play a causal role in COVID-19 severity. Understanding how risk factors impact COVID-19 susceptibility and severity will help us understand potential long-term effects in different patient populations.

Reference

https://www.cell.com/cell-stem-cell/fulltext/S1934-5909(20)30602-0

Physical distancing and risk of COVID-19 in small-scale fisheries: A remote sensing assessment in coastal Ghana

Abstract

The novel coronavirus is predicted to have dire implications on global food systems including fisheries value chains due to restrictions imposed on human movements in many countries. In Ghana, food production, both agriculture and fisheries, is exempted from restrictions as an essential service. The enforcement of COVID-19 prevention protocols, particularly social distancing, has been widely reported in Ghana's agricultural markets whereas casual observations and media reports on fish landing sites suggest no such enforcements are in place. This study aimed to provide sound scientific evidence as a basis for informed policy direction and intervention for the artisanal fishing sector in these challenging times. An unmanned aerial vehicle was employed in assessing the risk of artisanal fishers to the pandemic using physical distancing as a proxy. From analysis

of cumulative distribution function (G-function) of the nearest-neighbour distances, this study underscored crowding at all surveyed fish landing beaches, and identified potential “hotspots” for disease transmission. Aerial measurements taken at times of peak landing beach activity indicated that the highest proportion of people, representing 56%, 48%, 39% and 78% in Elmina, Winneba, Apam and Mumford respectively, were located at distances of less than one metre from their nearest neighbour. Risk of crowding was independent of the population at the landing beaches, suggesting that all categories of fish landing sites along the coast would require equal urgency and measured attention towards preventing and mitigating the spread of the disease.

Reference

https://www.nature.com/articles/s41598-020-79898-4

Publication Date: Dec 28, 2020

In silico discovery of antigenic proteins and epitopes of SARS-CoV-2 for the development of a vaccine or a diagnostic approach for COVID-19

Abstract

In the genome of SARS-CoV-2, the 5′-terminus encodes a polyprotein, which is further cleaved into 15 non-structural proteins whereas the 3′ terminus encodes four structural proteins and eight accessory proteins. Among these 27 proteins, the present study aimed to discover likely antigenic proteins and epitopes to be used for the development of a vaccine or serodiagnostic assay using an in silico approach. For this purpose, after the full genome analysis of SARS-CoV-2 Wuhan isolate and variant proteins that are detected frequently, surface proteins including spike, envelope, and membrane proteins as well as proteins with signal peptide were determined as probable vaccine candidates whereas the remaining were considered as possible antigens to be used during the development of serodiagnostic assays. According to results obtained, among 27 proteins, 26 of them were predicted as probable antigen. In 26 proteins, spike protein was selected as the best vaccine candidate because of having a signal peptide, negative GRAVY value, one transmembrane helix, moderate aliphatic index, a big molecular weight, a long-estimated half-life, beta wrap motifs as well as having stable, soluble and non-allergic features. In addition, orf7a, orf8, and nsp-10 proteins with signal peptide were considered as potential

vaccine candidates. Nucleocapsid protein and a highly antigenic GGDGKMKD epitope were identified as ideal antigens to be used in the development of serodiagnostic assays. Moreover, considering MHC-I alleles, highly antigenic KLNDLCFTNV and ITLCFTLKRK epitopes can be used to develop an epitope-based peptide vaccine.

Reference

https://www.nature.com/articles/s41598-020-79645-9

Neonatal hyperoxia enhances age-dependent expression of SARS-CoV-2 receptors in mice

Abstract

The severity of COVID-19 lung disease is higher in the elderly and people with pre-existing co-morbidities. People who were born preterm may be at greater risk for COVID-19 because their early exposure to oxygen (hyperoxia) at birth increases the severity of respiratory viral infections. Hyperoxia at birth increases the severity of influenza A virus infections in adult mice by reducing the number of alveolar epithelial type 2 (AT2) cells. Since AT2 cells express the SARS-CoV-2 receptors angiotensin converting enzyme (ACE2) and transmembrane protease/serine subfamily member 2 (TMPRSS2), their expression should decline as AT2 cells are depleted by hyperoxia. Instead, ACE2 was detected in airway Club cells and endothelial cells at birth, and then AT2 cells at one year of age. Neonatal hyperoxia stimulated expression of ACE2 in Club cells and in AT2 cells by 2 months of age. It also stimulated expression of TMPRSS2 in the lung. Increased expression of SARS-CoV-2 receptors was blocked by mitoTEMPO, a mitochondrial superoxide scavenger that reduced oxidative stress and DNA damage seen in oxygen-exposed mice. Our finding that hyperoxia enhances the age-dependent expression of SARS-CoV-2 receptors in mice helps explain why COVID-19 lung disease is greater in the elderly and people with pre-existing co-morbidities.

Reference

https://www.nature.com/articles/s41598-020-79595-2

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) membrane (M) protein inhibits type I and III interferon production by targeting RIG-I/MDA-5 signaling

Abstract

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has quickly spread worldwide and has affected more than 10 million individuals. A typical feature of COVID-19 is the suppression of type I and III interferon (IFN)-mediated antiviral immunity. However, the molecular mechanism by which SARS-CoV-2 evades antiviral immunity remains elusive. Here, it was reported that the SARS-CoV-2 membrane (M) protein inhibits the production of type I and III IFNs induced by the cytosolic dsRNA-sensing pathway mediated by RIG-I/MDA-5–MAVS signaling. In addition, the SARS-CoV-2 M protein suppresses type I and III IFN induction stimulated by SeV infection or poly (I:C) transfection. Mechanistically, the SARS-CoV-2 M protein interacts with RIG-I, MAVS, and TBK1, thus preventing the formation of the multiprotein complex containing RIG-I, MAVS, TRAF3, and TBK1 and subsequently impeding the phosphorylation, nuclear translocation, and activation of IRF3. Consequently, ectopic expression of the SARS-CoV-2 M protein facilitates the replication of vesicular stomatitis virus. Taken together, these results indicate that the SARS-CoV-2 M protein antagonizes type I and III IFN production by targeting RIG-I/MDA-5 signaling, which subsequently attenuates antiviral immunity and enhances viral replication. This study provides insight into the interpretation of SARS-CoV-2-induced antiviral immune suppression and illuminates the pathogenic mechanism of COVID-19.

Reference

https://www.nature.com/articles/s41392-020-00438-7

A meta-analysis of accuracy and sensitivity of chest CT and RT-PCR in COVID-19 diagnosis

Abstract

Nowadays there is an ongoing acute respiratory outbreak caused by the novel highly contagious coronavirus (COVID-19). The diagnostic protocol is based on quantitative reverse-transcription polymerase chain reaction (RT-PCR) and chests CT scan, with

uncertain accuracy. This meta-analysis study determines the diagnostic value of an initial chest CT scan in patients with COVID-19 infection in comparison with RT-PCR. Three main databases; PubMed (MEDLINE), Scopus, and EMBASE were systematically searched for all published literature from January 1st, 2019, to the 21st May 2020 with the keywords "COVID19 virus", "2019 novel coronavirus", "Wuhan coronavirus", "2019-nCoV", "X-Ray Computed Tomography", "Polymerase Chain Reaction", "Reverse Transcriptase PCR", and "PCR Reverse Transcriptase". All relevant case-series, cross-sectional, and cohort studies were selected. Data extraction and analysis were performed using STATA v.14.0SE (College Station, TX, USA) and RevMan 5. Among 1022 articles, 60 studies were eligible for totalizing 5744 patients. The overall sensitivity, specificity, positive predictive value, and negative predictive value of chest CT scan compared to RT-PCR were 87% (95% CI 85–90%), 46% (95% CI 29–63%), 69% (95% CI 56–72%), and 89% (95% CI 82–96%), respectively. It is important to rely on the repeated RT-PCR three times to give 99% accuracy, especially in negative samples. Regarding the overall diagnostic sensitivity of 87% for chest CT, the RT-PCR testing is essential and should be repeated to escape misdiagnosis.

Reference

https://www.nature.com/articles/s41598-020-80061-2

SalivaDirect: A simplified and flexible platform to enhance SARS-CoV-2 testing capacity

Abstract

Background: Scaling SARS-CoV-2 testing to meet demands of safe reopenings continues to be plagued by assay costs and supply chain shortages. In response, SalivaDirect was developed, which received Emergency Use Authorization (EUA) from the U.S. FDA.

Methods: Saliva-based diagnostic test was by simplified not requiring collection tubes with preservatives, replacing nucleic acid extraction with a simple enzymatic and heating step, and testing specimens with a dualplex RT-qPCR assay. Moreover, SalivaDirect was validated with reagents and instruments from multiple vendors to minimize supply chain issues.

Findings: From our hospital cohort, a high positive agreement (94%) was shown between saliva tested with SalivaDirect and nasopharyngeal swabs tested with a commercial RT-qPCR kit. In partnership with the National Basketball Association and Players Association, we tested 3,779 saliva specimens from healthy individuals, and detected low rates of invalid (0.3%) and false positive (<0.05%) results.

Conclusions: It was demonstrated that saliva is a valid alternative to swabs for SARS-CoV-2 screening, and that SalivaDirect can make large-scale testing more accessible and affordable. Uniquely, other laboratories was designated to use our sensitive, flexible, and simplified platform under our EUA: HYPERLINK "https://publichealth.yale.edu/salivadirect/" \o "https://publichealth.yale.edu/salivadirect/" \h publichealth.yale.edu/salivadirect/.

Reference

https://www.cell.com/med/fulltext/S2666-6340(20)30076-3

Publication Date: Dec 26, 2020

High-throughput rational design of the remdesivir binding site in the RdRp of SARS-CoV-2: Implications for potential resistance

Abstract

The use of remdesivir to treat COVID-19 will likely continue before clinical trials are completed. Due to the lengthening pandemic and evolving nature of the virus, predicting potential residues prone to mutation is crucial for the management of remdesivir resistance. Using a rational ligand-based interface design complemented with mutational mapping, we generated a total of 100,000 mutations and provided insight into the functional outcomes of mutations in the remdesivir-binding site in nsp12 subunit of RdRp. After designing 46 residues in the remdesivir-binding site of nsp12, the designs retained 97-98% sequence identity, suggesting that very few mutations in nsp12 are required for SARS-CoV-2 to attain remdesivir resistance. Several mutants displayed decreased binding affinity to remdesivir, suggesting drug resistance. These hotspot residues had a higher probability of undergoing selective mutation and thus conferring remdesivir resistance. Identifying the potential residues prone to mutation improves our understanding of SARS-CoV-2 drug resistance and COVID-19 pathogenesis.

Reference

https://www.cell.com/iscience/fulltext/S2589-0042(20)31189-5

Attitudes towards vaccines and intention to vaccinate against COVID-19: Implications for public health communications

Abstract

Background: Negative attitudes towards vaccines and an uncertainty or unwillingness to receive vaccinations are major barriers to managing the COVID-19 pandemic in the long-term. We estimate predictors of four domains of negative attitudes towards vaccines and identify groups most at risk of uncertainty and unwillingness to receive a COVID-19 vaccine in a large sample of UK adults.

Methods: Data were cross-sectional and from 32,361 adults in the UCL COVID-19 Social Study. Ordinary least squares regression analyses examined the impact of socio-demographic and COVID-19 related factors on four types of negative vaccine attitudes: mistrust of vaccine benefit, worries about unforeseen effects, concerns about commercial profiteering, and preference for natural immunity. Multinomial regression examined the impact of socio-demographic and COVID-19 related factors, negative vaccine attitudes, and prior vaccine behaviour on uncertainty and unwillingness to be vaccinated for COVID-19.

Findings: 16% of respondents displayed high levels of mistrust about vaccines across one or more domains. Distrustful attitudes towards vaccination were higher amongst individuals from ethnic minority backgrounds, with lower levels of education, lower annual income, poor knowledge of COVID-19, and poor compliance with government COVID-19 guidelines. Overall, 14% of respondents reported unwillingness to receive a vaccine for COVID-19, whilst 23% were unsure. The largest predictors of both COVID-19 vaccine uncertainty and refusal were low-income groups (< £16,000, a year), having not received a flu vaccine last year, poor adherence to COVID-19 government guidelines, female gender, and living with children. Amongst vaccine attitudes, intermediate to high levels of mistrust of vaccine benefit and concerns about future unforeseen side effects were the most important determinants of both uncertainty and unwillingness to vaccinate against COVID-19.

Interpretation: Negative attitudes towards vaccines are a major public health concern in the UK. General mistrust in vaccines and concerns about future side effects in particular will be barriers to achieving population immunity to COVID-19 through vaccination. Public health messaging should be tailored to address these concerns and specifically to women, ethnic minorities, and people with lower levels of education and incomes.

Reference

https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762(20)30012-0/fulltext

Publication Date: Dec 25, 2020

Induction of alarmin S100A8/A9 mediates activation of aberrant neutrophils in the pathogenesis of COVID-19

Abstract

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic poses an unprecedented public health crisis. Evidence suggests that SARS-CoV-2 infection causes dysregulation of the immune system. However, the unique signature of early immune responses remains elusive. We characterized the transcriptome of rhesus macaques and mice infected with SARS-CoV-2. Alarmin S100A8 was robustly induced in SARS-CoV-2-infected animal models as well as in COVID-19 patients. Paquinimod, a specific inhibitor of S100A8/A9, could rescue the pneumonia with substantial reduction of viral loads in SARS-CoV-2-infected mice. Remarkably, Paquinimod treatment resulted in almost 100% survival in a lethal model of mouse coronavirus infection using the mouse hepatitis virus (MHV). A group of neutrophils that contributes to the uncontrolled pathological damage and onset of COVID-19 was dramatically induced by coronavirus infection. Paquinimod treatment could reduce these neutrophils and regain anti-viral responses, unveiling key roles of S100A8/A9 and aberrant neutrophils in the pathogenesis of COVID-19, highlighting new opportunities for therapeutic intervention.

Reference

https://www.cell.com/cell-host-microbe/fulltext/S1931-3128(20)30679-X

Atlas of ACE2 gene expression reveals novel insights into transmission of SARS-CoV-2

Abstract

The recent pandemic, COVID-19, is caused by a novel coronavirus, SARS-CoV-2, with elusive origin. SARS-CoV-2 infects mammalian cells via ACE2, a transmembrane protein. Therefore, the conservation and expression patterns of ACE2 may provide valuable insights into tracing the carriers of SARS-CoV-2. In this work, the conservation of ACE2 and its expression pattern was analyzed among various mammalian species that are close to human beings. It was shown that mammalian ACE2 gene is deeply conserved at both DNA and peptide levels, suggesting that a broad range of mammals can potentially host SARS-CoV-2. It was further reported that ACE2 expression in certain human tissues are consistent with clinical symptoms of COVID-19 patients. Furthermore, the first atlas of ACE2 expression was built in various common mammals, which shows that ACE2 expresses in mammalian tissues in a species-specific manner. Most notably, exceptionally high expression of ACE2 was observed in external body parts of cats and dogs, suggesting that these household pet animals could be vulnerable to viral infections and/or may serve as intermediate hosts, thus yielding novel insights into the transmission of SARS-CoV-2.

Reference

https://www.cell.com/heliyon/fulltext/S2405-8440(20)32692-X

A distinct innate immune signature marks progression from mild to severe COVID-19

Abstract

Coronavirus disease 2019 (COVID-19) manifests with a range of severities, but immune signatures of mild and severe disease are still not fully understood. Mass cytometry and targeted proteomics was used to profile the innate immune response of patients with mild or severe COVID-19 and of healthy individuals. Sampling at different stages allows us to reconstruct a pseudo-temporal trajectory of the innate response. A surge of CD169+ monocytes associated with an IFNγ+MCP-2+ signature rapidly follows symptom onset. At later stages, we observe a persistent inflammatory phenotype in patients with severe

disease, dominated by high CCL3 and CCL4 abundance correlating with the re-appearance of CD16+ monocytes, whereas the response of mild COVID-19 patients normalizes. The data provide insights into the dynamic nature of inflammatory responses in COVID-19 patients and identify sustained innate immune responses as a likely mechanism in severe patients, thus supporting investigation of targeted interventions in severe COVID-19.

Reference

https://www.cell.com/cell-reports-medicine/fulltext/S2666-3791(20)30213-5

D614G mutation alters SARS-CoV-2 spike conformation and enhances protease cleavage at the S1/S2 junction

Abstract

The SARS-CoV-2 spike (S) protein is the target of vaccine design efforts to end the COVID-19 pandemic. Despite a low mutation rate, isolates with the D614G substitution in the S protein appeared early during the pandemic, and are now the dominant form worldwide. Here, we explore spike conformational changes and the effects of the D614G mutation on a soluble S ectodomain construct. Cryo-EM structures reveal altered RBD disposition; antigenicity and proteolysis experiments reveal structural changes and enhanced furin cleavage efficiency of the G614 variant. Furthermore, furin cleavage alters the up/down ratio of the Receptor Binding Domains (RBD) in the G614 S ectodomain, demonstrating an allosteric effect on RBD positioning triggered by changes in the SD2 region, that harbors residue 614 and the furin cleavage site. Our results elucidate SARS-CoV-2 spike conformational landscape and allostery, and have implications for vaccine design. For more details, read the link given below.

Reference

https://www.cell.com/cell-reports/fulltext/S2211-1247(20)31619-3

Hypertension delays viral clearance and exacerbates airway hyperinflammation in patients with COVID-19

Abstract

In coronavirus disease 2019 (COVID-19), hypertension and cardiovascular diseases are major risk factors for critical disease progression. However, the underlying causes and the effects of the main anti-hypertensive therapies—angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs)—remain unclear. Combining clinical data (n = 144) and single-cell sequencing data of airway samples (n = 48) with in vitro experiments, we observed a distinct inflammatory predisposition of immune cells in patients with hypertension that correlated with critical COVID-19 progression. ACEI treatment was associated with dampened COVID-19-related hyperinflammation and with increased cell intrinsic antiviral responses, whereas ARB treatment related to enhanced epithelial–immune cell interactions. Macrophages and neutrophils of patients with hypertension, in particular under ARB treatment, exhibited higher expression of the pro-inflammatory cytokines CCL3 and CCL4 and the chemokine receptor CCR1. Although the limited size of our cohort does not allow us to establish clinical efficacy, our data suggest that the clinical benefits of ACEI treatment in patients with COVID-19 who have hypertension warrant further investigation.

Reference

https://www.nature.com/articles/s41587-020-00796-1

Longitudinal transcriptome analyses show robust T cell immunity during recovery from COVID-19

Abstract

Understanding the processes of immune regulation in patients infected with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is crucial for improving treatment. Here, longitudinal whole-transcriptome RNA sequencing was performed on peripheral blood mononuclear cell (PBMC) samples from 18 patients with coronavirus disease 2019 (COVID-19) during their treatment, convalescence, and rehabilitation. After

analyzing the regulatory networks of differentially expressed messenger RNAs (mRNAs), microRNAs (miRNAs) and long non-coding RNAs (lncRNAs) between the different clinical stages, we found that humoral immunity and type I interferon response were significantly downregulated, while robust T-cell activation and differentiation at the whole transcriptome level constituted the main events that occurred during recovery from COVID-19. The formation of this T cell immune response might be driven by the activation of activating protein-1 (AP-1) related signaling pathway and was weakly affected by other clinical features. These findings uncovered the dynamic pattern of immune responses and indicated the key role of T cell immunity in the creation of immune protection against this disease.

Reference

https://www.nature.com/articles/s41392-020-00457-4

Endothelial activation and dysfunction in COVID-19: From basic mechanisms to potential therapeutic approaches

Abstract

On 12 March 2020, the outbreak of coronavirus disease 2019 (COVID-19) was declared a pandemic by the World Health Organization. As of 4 August 2020, more than 18 million confirmed infections had been reported globally. Most patients have mild symptoms, but some patients develop respiratory failure which is the leading cause of death among COVID-19 patients. Endothelial cells with high levels of angiotensin-converting enzyme 2 expression are major participants and regulators of inflammatory reactions and coagulation. Accumulating evidence suggests that endothelial activation and dysfunction participate in COVID-19 pathogenesis by altering the integrity of vessel barrier, promoting pro-coagulative state, inducing endothelial inflammation, and even mediating leukocyte infiltration. This review describes the proposed cellular and molecular mechanisms of endothelial activation and dysfunction during COVID-19 emphasizing the principal mediators and therapeutic implications.

Reference

https://www.nature.com/articles/s41392-020-00454-7

Publication Date: Dec 24, 2020

The brain after COVID-19: Compensatory neurogenesis or persistent neuroinflammation?

Regional volume increase and decreased diffusivity may reflect persistent neuroinflammation rather than neurogenesis. Viral neuro-infections cause inflammatory states, activating several CNS cell types and causing edema, leading to transient increases in regional brain volume.

Yiping Lu *et al.* report increased grey matter volumes and changes in MRI-based measures of water diffusion in white matter in the brains of recovered COVID-19 patients three months after acute illness, compared to healthy controls. They propose that neurogenesis and hypertrophy caused volumetric enlargement, and pathway remyelination restricted diffusion in the patients. If valid, these explanations suggest vigorous and counter-intuitive compensatory brain mechanisms during recovery from COVID-19. However, both the methodology and the findings of the study allow alternative explanations. The samples were matched for age and sex, but not for educational or premorbid neurocognitive variables known to correlate with microstructural and volumetric variables. This allows the possibility that the patient sample included larger and more interconnected premorbid brains than the control sample. For more details, read the link given below.

Reference

https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(20)30428-4/fulltext

Letter regarding 'Ethnicity and clinical outcomes in COVID-19: A systematic review and meta-analysis'

Social distancing restrictions, community-wide lockdowns, and the wearing of personal protective equipment have been implemented globally in attempts to contain the spread of SARS-CoV-2, reflecting the knowledge that prolonged physical proximity and verbal interaction between individuals increases the likelihood of viral transmission. Accordingly, key risk factors such as population density, occupational exposure, and household size

must be taken into account when comparing the risk of COVID-19 infection between groups. Despite this, there was little consistency in the adjustments made for confounders in the studies included in this meta-analysis, with many making no adjustments whatsoever. The smaller effect sizes in the adjusted analyses compared to the unadjusted analyses highlight the importance of these confounding factors, and underscore the paramount importance of collecting, reporting, and including such data in statistical investigations of this nature. Clarity on this matter is urgently required as calls are made to consider ethnicity in the prioritisation of COVID-19 vaccine allocation, and structural racism is hypothesised to contribute to an increased risk of poor clinical outcomes in ethnic minority groups. For more details, read the link given below.

Reference

https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(20)30429-6/fulltext

Publication Date: Dec 28, 2020

Novavax launches pivotal U.S. trial of dark horse COVID-19 vaccine after manufacturing delays

Novavax, a once-struggling biotech company that was rescued by $2 billion in funding for its promising COVID-19 vaccine candidate from the Coalition for Epidemic Preparedness Innovations and the U.S. government, announced today the long-awaited start of its U.S. efficacy trial. Novavax has already fully enrolled an efficacy trial in the United Kingdom with more than 15,000 volunteers, whose data it plans to use to support its application for European regulatory approval.

Novavax's COVID-19 candidate is one of two protein subunit vaccines—the other is made by the vaccinemaking giant Sanofi Pasteur—on which the U.S. government has bet billions of dollars, and the first to enter a pivotal efficacy trial. It consists of tiny lipid particles studded with copies of the spike protein from the pandemic coronavirus SARS-CoV-2. The vaccine's lipids do not contain the polymer polyethylene glycol that has raised allergic reaction concerns for other COVID-19 vaccine, but it is supplemented by an immune-boosting, plant-derived compound called a saponin. Two-thirds of up to 30,000 volunteers in the North American placebo-controlled trial will receive the active vaccine. There will be 108 U.S. trial sites and seven in Mexico. For more details, read the link given below.

Reference

https://www.sciencemag.org/news/2020/12/novavax-launches-pivotal-us-trial-dark-horse-covid-19-vaccine-after-manufacturing