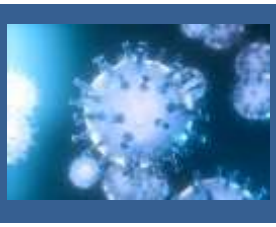
COVID-19

May 06 - 12, 2021



RESEARCH PUBLICATIONS

Publication Date: May 12, 2021

An artificial intelligence system for predicting the deterioration of COVID-19 patients in the emergency department

Abstract

During the coronavirus disease 2019 (COVID-19) pandemic, rapid and accurate triage of patients at the emergency department is critical to inform decision-making. A data-driven approach was proposed for automatic prediction of deterioration risk using a deep neural network that learns from chest X-ray images and a gradient boosting model that learns from routine clinical variables. The AI prognosis system, trained using data from 3661 patients, achieves an area under the receiver operating characteristic curve (AUC) of 0.786 (95% CI: 0.745–0.830) when predicting deterioration within 96 hours. The deep neural network extracts informative areas of chest X-ray images to assist clinicians in interpreting the predictions and performs comparably to two radiologists in a reader study. In order to verify performance in a real clinical setting, a preliminary version of the deep neural network was silently deployed at New York University Langone Health during the first wave of the pandemic, which produced accurate predictions in real-time. In summary, the findings demonstrate the potential of the proposed system for assisting front-line physicians in the triage of COVID-19 patients.

Reference

https://www.nature.com/articles/s41746-021-00453-0

Evaluating social and spatial inequalities of large scale rapid lateral flow SARS-CoV-2 antigen testing in COVID-19 management: An observational study of Liverpool, UK (November 2020 to January 2021)

Abstract

Background: Large-scale asymptomatic testing of communities in Liverpool (UK) for SARS-CoV-2 was used as a public health tool for containing COVID-19. The aim of the study is to explore social and spatial inequalities in uptake and case-detection of rapid lateral flow SARS-CoV-2 antigen tests (LFTs) offered to people without symptoms of COVID-19.

Methods: Linked pseudonymised records for asymptomatic residents in Liverpool who received a LFT for COVID-19 between 6th November 2020 to 31st January 2021 were accessed using the Combined Intelligence for Population Health Action resource. Bayesian Hierarchical Poisson Besag, York, and Mollié models were used to estimate ecological associations for uptake and positivity of testing.

Findings: 214 525 residents (43%) received a LFT identifying 5192 individuals as positive cases of COVID-19 (1.3% of tests were positive). Uptake was highest in November when there was military assistance. High uptake was observed again in the week preceding Christmas and was sustained into a national lockdown. Overall uptake were lower among males (e.g. 40% uptake over the whole period), Black Asian and other Minority Ethnic groups (e.g. 27% uptake for 'Mixed' ethnicity) and in the most deprived areas (e.g. 32% uptake in most deprived areas). These population groups were also more likely to have received positive tests for COVID-19. Models demonstrated that uptake and repeat testing were lower in areas of higher deprivation, areas located further from test sites and areas containing populations less confident in the using Internet technologies. Positive tests were spatially clustered in deprived areas.

Interpretation: Large-scale voluntary asymptomatic community testing saw social, ethnic, digital and spatial inequalities in uptake. COVID-19 testing and support to isolate need to be more accessible to the vulnerable communities most impacted by the pandemic, including non-digital means of access.

Reference

https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762(21)00084-3/fulltext

Clinical course and risk factors of fatal adverse outcomes in COVID-19 patients in Korea: A nationwide retrospective cohort study

Abstract

An association between epidemiological and clinical characteristics of coronavirus disease 2019 (COVID-19) patients and clinical outcomes in Korea was investigated. This nationwide retrospective cohort study included 5621 discharged patients with COVID-19, extracted from the Korea Disease Control and Prevention Agency (KDCA) database. We compared clinical data between survivors (n = 5387) and non-survivors (n = 234). We used logistic regression analysis and Cox proportional hazards model to explore risk factors of death and fatal adverse outcomes. Increased odds ratio (OR) of mortality occurred with age (≥ 60 years) [OR 11.685, 95% confidence interval (CI) 4.655–34.150, $p < 0.001$], isolation period, dyspnoea, altered mentality, diabetes, malignancy, dementia, and intensive care unit (ICU) admission. The multivariable regression equation including all potential variables predicted mortality (AUC = 0.979, 95% CI 0.964–0.993). Cox proportional hazards model showed increasing hazard ratio (HR) of mortality with dementia (HR 6.376, 95% CI 3.736–10.802, $p < 0.001$), ICU admission (HR 4.233, 95% CI 2.661–6.734, $p < 0.001$), age ≥ 60 years (HR 3.530, 95% CI 1.664–7.485, $p = 0.001$), malignancy (HR 3.054, 95% CI 1.494–6.245, $p = 0.002$), and dyspnoea (HR 1.823, 95% CI 1.125–2.954, $p = 0.015$). Presence of dementia, ICU admission, age ≥ 60 years, malignancy, and dyspnoea could help clinicians identify COVID-19 patients with poor prognosis.

Reference

https://www.nature.com/articles/s41598-021-89548-y

Evaluating social and spatial inequalities of large scale rapid lateral flow SARS-CoV-2 antigen testing in COVID-19 management: An observational study of Liverpool, UK (November 2020 to January 2021)

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Reference

https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762(21)00084-3/fulltext

Low SARS-CoV-2 seroprevalence in the Austrian capital after an early governmental lockdown

Abstract

SARS-CoV-2 seroprevalence in a large, well-described representative Viennese cohort was analyzed after an early governmental lockdown with respect to the occurrence of symptoms and household transmission. Participants of the LEAD Study, a population-based cohort study from Vienna, Austria, were invited along with their household members (April 20th to May20th 2020). Sera were analyzed using anti-SARS-CoV-2 immunoassay including a neutralization test as a confirmatory assay. A total of 12,419 individuals participated (5984 LEAD participants; 6435 household members), 163 (1.31%; 59 LEAD cohort members) of whom were SARS-CoV-2 antibody positive. The estimated number of COVID-19 cases projected from our findings by age and sex for Vienna was 21,504 (1.13%). Cumulative number of positively tested cases in Vienna until May 20th 2020 was 3020, hence 7.1 times (95% confidence interval 5.5–9.1) lower than projected. Relative risk (RR) of seropositivity by age was highest for children aged 6–9 years [RR compared to age group 20–49: 1.21 (CI 0.37–4.01)], lowest for ≥ 65 years [RR 0.47 (CI 0.21–1.03)]. Half of the positive individuals developed no or mild symptoms. In a multivariate analysis, taste and smell disturbances were most strongly related to SARS-CoV-2 positivity. Infection probability within households with one confirmed SARS-CoV-2-specific antibody-positive person was 31%. Although seroprevalence was very low (1.13%) for a central European capital city, due to an early governmental lockdown, SARS-CoV-2 infections were more prevalent than officially reported polymerase chain reaction-positive cases. Of note, seroprevalence was highest in young children. Half of SARS-CoV-2 antibody-positive subjects had no or only mild symptoms. Taste and smell disturbances were most prominent, possibly guiding clinicians in diagnosing SARS-CoV-2 infection.

Reference

https://www.nature.com/articles/s41598-021-89711-5

Effects of different types of written vaccination information on COVID-19 vaccine hesitancy in the UK (OCEANS-III): A single-blind, parallel-group, randomised controlled trial

Abstract

Background: The effectiveness of the COVID-19 vaccination programme depends on mass participation: the greater the number of people vaccinated, the less risk to the population. Concise, persuasive messaging is crucial, particularly given substantial levels of vaccine hesitancy in the UK. The aim was to test which types of written information about COVID-19 vaccination, in addition to a statement of efficacy and safety, might increase vaccine acceptance.

Methods: For this single-blind, parallel-group, randomised controlled trial, we aimed to recruit 15 000 adults in the UK, who were quota sampled to be representative. Participants were randomly assigned equally across ten information conditions stratified by level of vaccine acceptance (willing, doubtful, or strongly hesitant). The control information condition comprised the safety and effectiveness statement taken from the UK National Health Service website; the remaining conditions addressed collective benefit, personal benefit, seriousness of the pandemic, and safety concerns. After online provision of vaccination information, participants completed the Oxford COVID-19 Vaccine Hesitancy Scale (outcome measure; score range 7–35) and the Oxford Vaccine Confidence and Complacency Scale (mediation measure). The primary outcome was willingness to be vaccinated. Participants were analysed in the groups they were allocated. p values were adjusted for multiple comparisons. The study was registered with ISRCTN, ISRCTN37254291.

Findings: From Jan 19 to Feb 5, 2021, 15 014 adults were recruited. Vaccine hesitancy had reduced from 26·9% the previous year to 16·9%, so recruitment was extended to Feb 18 to recruit 3841 additional vaccine-hesitant adults. 12 463 (66·1%) participants were classified as willing, 2932 (15·6%) as doubtful, and 3460 (18·4%) as strongly hesitant (ie, report that they will avoid being vaccinated for as long as possible or will never get vaccinated). Information conditions did not alter COVID-19 vaccine hesitancy in those willing or doubtful (adjusted p values >0·70). In those strongly hesitant, COVID-19 vaccine hesitancy was reduced, in comparison to the control condition, by personal

benefit information (mean difference –1·49, 95% CI –2·16 to –0·82; adjusted p=0·0015), directly addressing safety concerns about speed of development (−0·91, –1·58 to –0·23; adjusted p=0·0261), and a combination of all information (−0·86, –1·53 to –0·18; adjusted p=0·0313). In those strongly hesitant, provision of personal benefit information reduced hesitancy to a greater extent than provision of information on the collective benefit of not personally getting ill (−0·97, 95% CI –1·64 to –0·30; adjusted p=0·0165) or the collective benefit of not transmitting the virus (−1·01, –1·68 to –0·35; adjusted p=0·0150). Ethnicity and gender were found to moderate information condition outcomes.

Interpretation: In the approximately 10% of the population who are strongly hesitant about COVID-19 vaccines, provision of information on personal benefit reduces hesitancy to a greater extent than information on collective benefits. Where perception of risk from vaccines is most salient, decision making becomes centred on the personal. As such, messaging that stresses the counterbalancing personal benefits is likely to prove most effective. The messaging from this study could be used in public health communications. Going forwards, the study highlights the need for future health campaigns to engage with the public on the terrain that is most salient to them.

Reference

https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667(21)00096-7/fulltext

Structural basis for broad coronavirus neutralization

Abstract

Three highly pathogenic β-coronaviruses have crossed the animal-to-human species barrier in the past two decades: SARS-CoV, MERS-CoV and SARS-CoV-2. To evaluate the possibility of identifying antibodies with broad neutralizing activity, we isolated a monoclonal antibody, termed B6, that cross-reacts with eight β-coronavirus spike glycoproteins, including all five human-infecting β-coronaviruses. B6 broadly neutralizes entry of pseudotyped viruses from lineages A and C, but not from lineage B, and the latter includes SARS-CoV and SARS-CoV-2. Cryo-EM, X-ray crystallography and membrane fusion assays reveal that B6 binds to a conserved cryptic epitope located in the fusion machinery. The data indicate that antibody binding sterically interferes with the spike conformational changes leading to membrane fusion. Our data provide a

structural framework explaining B6 cross-reactivity with β-coronaviruses from three lineages, along with a proof of concept for antibody-mediated broad coronavirus neutralization elicited through vaccination. This study unveils an unexpected target for next-generation structure-guided design of a pan-β-coronavirus vaccine.

Reference

https://www.nature.com/articles/s41594-021-00596-4

The interferon-stimulated exosomal hACE2 potently inhibits SARS-CoV-2 replication through competitively blocking the virus entry

Abstract

Since the outbreak of coronavirus disease 2019 (COVID-19), it has become a global pandemic. The spike (S) protein of etiologic severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) specifically recognizes human angiotensin-converting enzyme 2 (hACE2) as its receptor, which is recently identified as an interferon (IFN)-stimulated gene. Here, we find that hACE2 exists on the surface of exosomes released by different cell types, and the expression of exosomal hACE2 is increased by IFNα/β treatment. In particular, exosomal hACE2 can specifically block the cell entry of SARS-CoV-2, subsequently inhibit the replication of SARS-CoV-2 in vitro and ex vivo. Our findings have indicated that IFN is able to upregulate a viral receptor on the exosomes which competitively block the virus entry, exhibiting a potential antiviral strategy.

Reference

https://www.nature.com/articles/s41392-021-00604-5

The epidemicity index of recurrent SARS-CoV-2 infections

Abstract

Several indices can predict the long-term fate of emerging infectious diseases and the effect of their containment measures, including a variety of reproduction numbers (e.g. R_0R_0). Other indices evaluate the potential for transient increases of epidemics eventually doomed to disappearance, based on generalized reactivity analysis. They identify conditions for perturbations to a stable disease-free equilibrium ($R_0<1R_0<1$) to grow, possibly causing significant damage. Here, we introduce the epidemicity index e_0,

a threshold-type indicator: if $e_0 > 0$, initial foci may cause infection peaks even if $R_0<1R_0<1$. Therefore, effective containment measures should achieve a negative epidemicity index. We use spatially explicit models to rank containment measures for projected evolutions of the ongoing pandemic in Italy. There, we show that, while the effective reproduction number was below one for a sizable timespan, epidemicity remained positive, allowing recurrent infection flare-ups well before the major epidemic rebounding observed in the fall.

Reference

https://www.nature.com/articles/s41467-021-22878-7

Rapid and accurate agglutination-based testing for SARS-CoV-2 antibodies

Abstract

A rapid, accurate, and cost-effective serologic test was developed for SARS-CoV-2 virus, which caused the COVID-19 pandemic, on the basis of antibody-dependent agglutination of antigen-coated latex particles. When validated using plasma samples that are positive or negative for SARS-CoV-2, the agglutination assay detected antibodies against the receptor-binding domain of the spike (S-RBD) or the nucleocapsid protein of SARS-CoV-2 with 100% specificity and ~98% sensitivity. Furthermore, it was found that the strength of the S-RBD antibody response measured by the agglutination assay correlated with the efficiency of the plasma in blocking RBD binding to the angiotensin-converting enzyme 2 in a surrogate neutralization assay, suggesting that the agglutination assay might be used to identify individuals with virus-neutralizing antibodies. Intriguingly, it was found that >92% of patients had detectable antibodies on the day of a positive viral RNA test, suggesting that the agglutination antibody test might complement RNA testing for the diagnosis of SARS-CoV-2 infection.

Reference

https://www.cell.com/cell-reports-methods/fulltext/S2667-2375(21)00011-4

Mapping the SARS-CoV-2 spike glycoprotein-derived peptidome presented by HLA class II on dendritic cells

Abstract

Understanding and eliciting protective immune responses to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is an urgent priority. To facilitate these objectives, we profile the repertoire of human leukocyte antigen class II (HLA-II)-bound peptides presented by HLA-DR diverse monocyte-derived dendritic cells pulsed with SARS-CoV-2 spike (S) protein. 209 Unique HLA-II-bound peptide sequences were identified, many forming nested sets, which map to sites throughout S including glycosylated regions. Comparison of the glycosylation profile of the S protein to that of the HLA-II-bound S peptides reveals substantial trimming of glycan residues on the latter, likely induced during antigen processing. The data also highlight the receptor-binding motif in S1 as a HLA-DR-binding peptide-rich region and identify S2-derived peptides with potential for targeting by cross-protective vaccine-elicited responses. Results from this study will aid analysis of CD4+ T cell responses in infected individuals and vaccine recipients and have application in next-generation vaccine design.

Reference

https://www.cell.com/cell-reports/fulltext/S2211-1247(21)00524-6

Development of potent and selective inhibitors targeting the papain-like protease of SARS-CoV-2

Abstract

COVID-19 pandemic has been disastrous to society and effective drugs are urgently needed. The papain-like protease domain (PLpro) of SARS-CoV-2 (SCoV2) is indispensable for viral replication and represents a putative target for pharmacological intervention. In this work, we describe the development of a potent and selective SCoV2 PLpro inhibitor. The inhibitor not only effectively blocks substrate cleavage and immunosuppressive function imparted by PLpro, but also markedly mitigates SCoV2 replication in human cells, with a submicromolar IC_{50}. A convenient and sensitive activity probe was further presented, and complementary assays to readily evaluate

SCoV2 PLpro inhibitors in vitro or in cells. In addition, we disclose the co-crystal structure of SCoV2 PLpro in complex with a prototype inhibitor, which illuminates their detailed binding mode. Overall, these findings provide promising leads and important tools for drug discovery aiming to target SCoV2 PLpro.

Reference

https://www.cell.com/cell-chemical-biology/fulltext/S2451-9456(21)00213-0

Neutralizing antibody responses to SARS-CoV-2 in symptomatic COVID-19 is persistent and critical for survival

Abstract

Understanding how antibody responses to SARS-CoV-2 evolve during infection may provide important insight into therapeutic approaches and vaccination for COVID-19. Here we profile the antibody responses of 162 COVID-19 symptomatic patients in the COVID-BioB cohort followed longitudinally for up to eight months from symptom onset to find SARS-CoV-2 neutralization, as well as antibodies either recognizing SARS-CoV-2 spike antigens and nucleoprotein, or specific for S2 antigen of seasonal beta-coronaviruses and hemagglutinin of the H1N1 flu virus. The presence of neutralizing antibodies within the first weeks from symptoms onset correlates with time to a negative swab result ($p = 0.002$), while the lack of neutralizing capacity correlates with an increased risk of a fatal outcome ($p = 0.008$). Neutralizing antibody titers progressively drop after 5–8 weeks but are still detectable up to 8 months in the majority of recovered patients regardless of age or co-morbidities, with IgG to spike antigens providing the best correlate of neutralization. Antibody responses to seasonal coronaviruses are temporarily boosted, and parallel those to SARS-CoV-2 without dampening the specific response or worsening disease progression. Our results thus suggest compromised immune responses to the SARS-CoV-2 spike to be a major trait of COVID-19 patients with critical conditions, and thereby inform on the planning of COVID-19 patient care and therapy prioritization.

Reference

https://www.nature.com/articles/s41467-021-22958-8

A SARS-CoV-2 neutralizing antibody with extensive Spike binding coverage and modified for optimal therapeutic outcomes

Abstract

COVID-19 pandemic caused by SARS-CoV-2 constitutes a global public health crisis with enormous economic consequences. Monoclonal antibodies against SARS-CoV-2 can provide an important treatment option to fight COVID-19, especially for the most vulnerable populations. In this work, potent antibodies binding to SARS-CoV-2 Spike protein were identified from COVID-19 convalescent patients. Among them, P4A1 interacts directly with and covers majority of the Receptor Binding Motif of the Spike Receptor-Binding Domain, shown by high-resolution complex structure analysis. We further demonstrate the binding and neutralizing activities of P4A1 against wild type and mutant Spike proteins or pseudoviruses. P4A1 was subsequently engineered to reduce the potential risk for Antibody-Dependent Enhancement of infection and to extend its half-life. The engineered antibody exhibits an optimized pharmacokinetic and safety profile, and it results in complete viral clearance in a rhesus monkey model of COVID-19 following a single injection. These data suggest its potential against SARS-CoV-2 related diseases.

Reference

https://www.nature.com/articles/s41467-021-22926-2

A SARS-CoV-2 antibody curbs viral nucleocapsid protein-induced complement hyperactivation

Abstract

Although human antibodies elicited by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) nucleocapsid (N) protein are profoundly boosted upon infection, little is known about the function of N-reactive antibodies. Herein, we isolate and profile a panel of 32 N protein-specific monoclonal antibodies (mAbs) from a quick recovery coronavirus disease-19 (COVID-19) convalescent patient who has dominant antibody responses to the SARS-CoV-2 N protein rather than to the SARS-CoV-2 spike (S) protein. The complex structure of the N protein RNA binding domain with the highest binding affinity mAb (nCoV396) reveals changes in the epitopes and antigen’s allosteric

regulation. Functionally, a virus-free complement hyperactivation analysis demonstrates that nCoV396 specifically compromises the N protein-induced complement hyperactivation, which is a risk factor for the morbidity and mortality of COVID-19 patients, thus laying the foundation for the identification of functional anti-N protein mAbs.

Reference

https://www.nature.com/articles/s41467-021-23036-9

RIG-I triggers a signaling-abortive anti-SARS-CoV-2 defense in human lung cells

Abstract

Efficient immune responses against viral infection are determined by sufficient activation of nucleic acid sensor–mediated innate immunity. Coronavirus disease 2019, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), remains an ongoing global pandemic. It is an urgent challenge to clarify the innate recognition mechanism to control this virus. Here it was shown that retinoic acid–inducible gene-I (RIG-I) sufficiently restrains SARS-CoV-2 replication in human lung cells in a type I/III interferon (IFN)-independent manner. RIG-I recognizes the 3′ untranslated region of the SARS-CoV-2 RNA genome via the helicase domains, but not the C-terminal domain. This new mode of RIG-I recognition does not stimulate its ATPase, thereby aborting the activation of the conventional mitochondrial antiviral-signaling protein-dependent pathways, which is in accordance with lack of cytokine induction. Nevertheless, the interaction of RIG-I with the viral genome directly abrogates viral RNA-dependent RNA polymerase mediation of the first step of replication. Consistently, genetic ablation of RIG-I allows lung cells to produce viral particles that expressed the viral spike protein. By contrast, the anti-SARS-CoV-2 activity was restored by all-trans retinoic acid treatment through upregulation of RIG-I protein expression in primary lung cells derived from patients with chronic obstructive pulmonary disease. Thus, our findings demonstrate the distinctive role of RIG-I as a restraining factor in the early phase of SARS-CoV-2 infection in human lung cells.

Reference

https://www.nature.com/articles/s41590-021-00942-0

Computational optimization of the SARS-CoV-2 receptor-binding-motif affinity for human ACE2

Abstract

The coronavirus SARS-CoV-2, that is responsible for the COVID-19 pandemic, and the closely related SARS-CoV coronavirus enter cells by binding at the human angiotensin converting enzyme 2 (hACE2). The stronger hACE2 affinity of SARS-CoV-2 has been connected with its higher infectivity. In this work, it was studied that hACE2 complexes with the receptor binding domains (RBDs) of the human SARS-CoV-2 and human SARS-CoV viruses, using all-atom molecular dynamics (MD) simulations and Computational Protein Design (CPD) with a physics-based energy function. The MD simulations identify charge-modifying substitutions between the CoV-2 and CoV RBDs, which either increase or decrease the hACE2 affinity of the SARS-CoV-2 RBD. The combined effect of these mutations is small, and the relative affinity is mainly determined by substitutions at residues in contact with hACE2. Many of these findings are in line and interpret recent experiments. Our CPD calculations redesign positions 455, 493, 494 and 501 of the SARS-CoV-2 RBM, which contact hACE2 in the complex and are important for ACE2 recognition. Sampling is enhanced by an adaptive importance sampling Monte Carlo method. Sequences with increased affinity replace CoV-2 glutamine by a negative residue at position 493, serine by nonpolar, aromatic or a threonine at position 494, and asparagine by valine or threonine at position 501. Substitutions at positions 455 and 501 have a smaller effect on affinity. Substitutions suggested by our design are seen in viral sequences encountered in other species, including bat and pangolin. The results might be used to identify potential virus strains with higher human infectivity and assist in the design of peptide-based or peptidomimetic compounds with the potential to inhibit SARS-CoV-2 binding at hACE2.

Reference

https://www.cell.com/biophysj/fulltext/S0006-3495(21)00390-8

Genomic variation, origin tracing and vaccine development of SARS-CoV-2: A systematic review

Abstract

COVID-19 has spread globally to over 200 countries with more than 40 million confirmed cases and one million deaths as of November 1, 2020. The SARS-CoV-2 virus, leading to COVID-19, shows extremely high rates of infectivity and replication, and can result in pneumonia, acute respiratory distress, or even mortality. SARS-CoV-2 has been found to be continue rapidly evolving, with several genomic variants emerging in different regions throughout the world. In addition, despite intensive study of the spike protein, its origin and molecular mechanisms in mediating host invasion are still only partially resolved. Finally, the repertoire of drugs for COVID-19 treatment is still limited, with several candidates still under clinical trial and no effective therapeutic yet reported. Although vaccines based on either DNA/mRNA or protein have been deployed, their efficacy against emerging variants requires ongoing study, with multivalent vaccines supplanting the first generation vaccines due to their low efficacy against new strains. Here, we provide a systematic review of studies on the epidemiology, immunological pathogenesis, molecular mechanisms and structural biology, as well as approaches for drug or vaccine development for SARS-CoV-2.

Reference

https://www.cell.com/the-innovation/fulltext/S2666-6758(21)00041-2

Plant-derived exosomal microRNAs inhibit lung inflammation induced by exosomes SARS-CoV-2 Nsp12

Abstract

Lung inflammation is a hallmark of coronavirus disease 2019 (COVID-19). In this study, it was shown that mice develop inflamed lung tissue after being administered exosomes released from the lung epithelial cells exposed to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Nsp12 and Nsp13 (exosomesNsp12Nsp13). Mechanistically, we show that exosomesNsp12Nsp13 are taken up by lung macrophages, leading to activation of nuclear factor κB (NF-κB) and the subsequent induction of an array of inflammatory cytokines. Induction of tumor necrosis factor

(TNF)-α, interleukin (IL)-6, and IL-1β from exosomesNsp12Nsp13-activated lung macrophages contributes to inducing apoptosis in lung epithelial cells. Induction of exosomesNsp12Nsp13-mediated lung inflammation was abolished with ginger exosome-like nanoparticle (GELN) microRNA (miRNA aly-miR396a-5p. The role of GELNs in inhibition of the SARS-CoV-2-induced cytopathic effect (CPE) was further demonstrated via GELN aly-miR396a-5p- and rlcv-miR-rL1-28-3p-mediated inhibition of expression of Nsp12 and spike genes, respectively. Taken together, our results reveal exosomesNsp12Nsp13 as potentially important contributors to the development of lung inflammation, and GELNs are a potential therapeutic agent to treat COVID-19.

Reference

https://www.cell.com/molecular-therapy-family/molecular-therapy/fulltext/S1525-0016(21)00257-4

Single-cell RNA sequencing of blood antigen-presenting cells in severe COVID-19 reveals multi-process defects in antiviral immunity

Abstract

COVID-19 can lead to life-threatening respiratory failure, with increased inflammatory mediators and viral load. Here, we perform single-cell RNA-sequencing to establish a high-resolution map of blood antigen-presenting cells (APCs) in 15 patients with moderate or severe COVID-19 pneumonia, at day 1 and day 4 post admission to intensive care unit or pulmonology department, as well as in 4 healthy donors. We generated a unique dataset of 81,643 APCs, including monocytes and rare dendritic cell (DC) subsets. We uncovered multi-process defects in antiviral immune defence in specific APCs from patients with severe disease: (1) increased pro-apoptotic pathways in plasmacytoid DCs (pDCs, key effectors of antiviral immunity), (2) a decrease of the innate sensors TLR9 and DHX36 in pDCs and CLEC9a+ DCs, respectively, (3) downregulation of antiviral interferon-stimulated genes in monocyte subsets and (4) a decrease of major histocompatibility complex (MHC) class II-related genes and MHC class II transactivator activity in cDC1c+ DCs, suggesting viral inhibition of antigen presentation. These novel mechanisms may explain patient aggravation and suggest strategies to restore the defective immune defence.

Reference

https://www.nature.com/articles/s41556-021-00681-2

Development and characterization of two equine formulations towards SARS-CoV-2 proteins for the potential treatment of COVID-19

Abstract

In the current global emergency due to SARS-CoV-2 outbreak, passive immunotherapy emerges as a promising treatment for COVID-19. Among animal-derived products, equine formulations are still the cornerstone therapy for treating envenomations due to animal bites and stings. Therefore, drawing upon decades of experience in manufacturing snake antivenom, we developed and preclinically evaluated two anti-SARS-CoV-2 polyclonal equine formulations as potential alternative therapy for COVID-19. We immunized two groups of horses with either S1 (anti-S1) or a mixture of S1, N, and SEM mosaic (anti-Mix) viral recombinant proteins. Horses reached a maximum anti-viral antibody level at 7 weeks following priming, and showed no major adverse acute or chronic clinical alterations. Two whole-IgG formulations were prepared via hyperimmune plasma precipitation with caprylic acid and then formulated for parenteral use. Both preparations had similar physicochemical and microbiological quality and showed ELISA immunoreactivity towards S1 protein and the receptor binding domain (RBD). The anti-Mix formulation also presented immunoreactivity against N protein. Due to high anti-S1 and anti-RBD antibody content, final products exhibited high *in vitro* neutralizing capacity of SARS-CoV-2 infection, 80 times higher than a pool of human convalescent plasma. Pre-clinical quality profiles were similar among both products, but clinical efficacy and safety must be tested in clinical trials. The technological strategy describe here can be adapted by other producers, particularly in low- and middle-income countries.

Reference

https://www.nature.com/articles/s41598-021-89242-z

ChAdOx1 nCoV-19 (AZD1222) vaccine candidate significantly reduces SARS-CoV-2 shedding in ferrets

Abstract

Vaccines against SARS-CoV-2 are likely to be critical in the management of the ongoing pandemic. A number of candidates are in Phase III human clinical trials, including ChAdOx1 nCoV-19 (AZD1222), a replication-deficient chimpanzee adenovirus-vectored vaccine candidate. In preclinical trials, the efficacy of ChAdOx1 nCoV-19 against SARS-CoV-2 challenge was evaluated in a ferret model of infection. Groups of ferrets received either prime-only or prime-boost administration of ChAdOx1 nCoV-19 via the intramuscular or intranasal route. All ChAdOx1 nCoV-19 administration combinations resulted in significant reductions in viral loads in nasal-wash and oral swab samples. No vaccine-associated adverse events were observed associated with the ChAdOx1 nCoV-19 candidate, with the data from this study suggesting it could be an effective and safe vaccine against COVID-19. The study also indicates the potential for intranasal administration as a way to further improve the efficacy of this leading vaccine candidate.

Reference

https://www.nature.com/articles/s41541-021-00315-6

Identification and characterization of a SARS-CoV-2 specific CD8+ T cell response with immunodominant features

Abstract

The COVID-19 pandemic caused by SARS-CoV-2 is a continuous challenge worldwide, and there is an urgent need to map the landscape of immunogenic and immunodominant epitopes recognized by CD8+ T cells. Here, samples from 31 patients with COVID-19 were analyzed for CD8+ T cell recognition of 500 peptide-HLA class I complexes, restricted by 10 common HLA alleles. 18 CD8+ T cell was identified and recognized SARS-CoV-2 epitopes, including an epitope with immunodominant features derived from ORF1ab and restricted by HLA-A*01:01. In-depth characterization of SARS-CoV-2-specific CD8+ T cell responses of patients with acute critical and severe disease reveals high expression of NKG2A, lack of cytokine production and a gene

expression profile inhibiting T cell re-activation and migration while sustaining survival. SARS-CoV-2-specific CD8+ T cell responses are detectable up to 5 months after recovery from critical and severe disease, and these responses convert from dysfunctional effector to functional memory CD8+ T cells during convalescence.

Reference

https://www.nature.com/articles/s41467-021-22811-y

Viral dynamics and antibody responses in people with asymptomatic SARS-CoV-2 infection

Abstract

Over 40% of the coronavirus disease 2019 (COVID-19) COVID-19 patients were asymptomatically infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the immune responses of these asymptomatic individuals is a critical factor for developing the strategy to contain the COVID-19 pandemic. Here, we determined the viral dynamics and antibody responses among 143 asymptomatic individuals identified in a massive screening of more than 5 million people in eight districts of Wuhan in May 2020. Asymptomatic individuals were admitted to the government-designated centralized sites in accordance with policy. The incidence rate of asymptomatic infection is ~2.92/100,000. These individuals had low viral copy numbers (peaked at 315 copies/mL) and short-lived antibody responses with the estimated diminish time of 69 days. The antibody responses in individuals with persistent SARS-CoV-2 infection is much longer with the estimated diminish time of 257 days. These results imply that the immune responses in the asymptomatic individuals are not potent enough for preventing SARS-CoV-2 re-infection, which has recently been reported in recovered COVID-19 patients. This casts doubt on the efficacy of forming “herd-immunity” through natural SARS-CoV-2 infection and urges for the development of safe and effective vaccines.

Reference

https://www.nature.com/articles/s41392-021-00596-2

Feasibility of large-scale population testing for SARS-CoV-2 detection by self-testing at home

Abstract

The simplicity and low cost of rapid point-of-care tests greatly facilitate large-scale population testing, which can contribute to controlling the spread of the COVID-19 virus. We evaluated the applicability of a self-testing strategy for SARS-CoV2 in a population-based, cross-sectional study in Cantabria, Spain, between April and May 2020. For the self-testing strategy, participants received the necessary material for the self-collection of blood and performance of a rapid antibody test using lateral flow immunoassay at home without the supervision of healthcare personnel. A total of 1,022 participants were enrolled. Most participants correctly performed the COVID-19 self-test the first time (91.3% [95% CI 89.4–92.9]). Only a minority of the participants (0.7%) needed the help of healthcare personnel, while 6.9% required a second kit delivery, for a total valid test result in 96.9% of the participants. Incorrect use of the self-test was not associated with the educational level, age over 65, or housing area. Prevalence of IgG antibodies against SARS-CoV2 for subjects with a valid rapid test result was 3.1% (95% CI 2.2–4.4), similar to the seroprevalence result obtained using a conventional approach carried out by healthcare professionals. In conclusion, COVID-19 self-testing should be considered as a screening tool.

Reference

https://www.nature.com/articles/s41598-021-89236-x

Post-acute effects of SARS-CoV-2 infection in individuals not requiring hospital admission: A Danish population-based cohort study

Abstract

Background: Individuals admitted to hospital for COVID-19 might have persisting symptoms (so-called long COVID) and delayed complications after discharge. However, little is known regarding the risk for those not admitted to hospital. Therefore prescription drug and health-care use was examined, after SARS-CoV-2 infection not requiring hospital admission.

Methods: This was a population-based cohort study using the Danish prescription, patient, and health insurance registries. All individuals with a positive or negative RT-PCR test for SARS-CoV-2 in Denmark between Feb 27 and May 31, 2020, were eligible for inclusion. Outcomes of interest were delayed acute complications, chronic disease, hospital visits due to persisting symptoms, and prescription drug use. We used data from non-hospitalised SARS-CoV-2-positive and matched SARS-CoV-2-negative individuals from 2 weeks to 6 months after a SARS-CoV-2 test to obtain propensity score-weighted risk differences (RDs) and risk ratios (RRs) for initiation of 14 drug groups and 27 hospital diagnoses indicative of potential post-acute effects. We also calculated prior event rate ratio-adjusted rate ratios of overall health-care use. This study is registered in the EU Electronic Register of Post-Authorisation Studies (EUPAS37658).

Findings: 10 498 Eligible individuals tested positive for SARS-CoV-2 in Denmark from Feb 27 to May 31, 2020, of whom 8983 (85·6%) were alive and not admitted to hospital 2 weeks after their positive test. The matched SARS-CoV-2-negative reference population not admitted to hospital consisted of 80 894 individuals. Compared with SARS-CoV-2-negative individuals, SARS-CoV-2-positive individuals were not at an increased risk of initiating new drugs (RD <0·1%) except bronchodilating agents, specifically short-acting β2-agonists (117 [1·7%] of 6935 positive individuals vs 743 [1·3%] of 57 206 negative individuals; RD +0·4% [95% CI 0·1–0·7]; RR 1·32 [1·09–1·60]) and triptans (33 [0·4%] of 8292 vs 198 [0·3%] of 72 828; RD +0·1% [0·0–0·3]; RR 1·55 [1·07–2·25]). There was an increased risk of receiving hospital diagnoses of dyspnoea (103 [1·2%] of 8676 vs 499 [0·7%] of 76 728; RD +0·6% [0·4–0·8]; RR 2·00 [1·62–2·48]) and venous thromboembolism (20 [0·2%] of 8785 vs 110 [0·1%] of 78 872; RD +0·1% [0·0–0·2]; RR 1·77 [1·09–2·86]) for SARS-CoV-2-positive individuals compared with negative individuals, but no increased risk of other diagnoses. Prior event rate ratio-adjusted rate ratios of overall general practitioner visits (1·18 [95% CI 1·15–1·22]) and outpatient hospital visits (1·10 [1·05–1·16]), but not hospital admission, showed increases among SARS-CoV-2-positive individuals compared with SARS-CoV-2-negative individuals.

Interpretation: The absolute risk of severe post-acute complications after SARS-CoV-2 infection not requiring hospital admission is low. However, increases in visits to general practitioners and outpatient hospital visits could indicate COVID-19 sequelae.

Reference

https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00211-5/fulltext

Publication Date: May 09, 2021

Dynamics of B cell repertoires and emergence of cross-reactive responses in patients with different severities of COVID-19

Abstract

Individuals with the 2019 coronavirus disease (COVID-19) show varying severity of the disease, ranging from asymptomatic to requiring intensive care. Although monoclonal antibodies specific to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have been identified, we still lack an understanding of the overall landscape of B cell receptor (BCR) repertoires in individuals with COVID-19. We use high-throughput sequencing of bulk and plasma B cells collected at multiple time points during infection to characterize signatures of the B cell response to SARS-CoV-2 in 19 individuals. Using principled statistical approaches, we associate differential features of BCRs with different disease severity. We identify 38 significantly expanded clonal lineages shared among individuals as candidates for responses specific to SARS-CoV-2. Using single-cell sequencing, the reactivity of BCRs shared among individuals was verified to SARS-CoV-2 epitopes. Moreover, the natural emergence of a BCR with cross-reactivity to SARS-CoV-1 and SARS-CoV-2 in some individuals was identified. The results provide insights important for development of rational therapies and vaccines against COVID-19.

Reference

https://www.cell.com/cell-reports/fulltext/S2211-1247(21)00518-0

Distinct immunological signatures discriminate severe COVID-19 from non-SARS-CoV-2-driven critical pneumonia

Abstract

Immune profiling of COVID-19 patients has identified numerous alterations in both innate and adaptive immunity. However, whether those changes are specific to SARS-CoV-2 or driven by a general inflammatory response shared across severely ill pneumonia patients remains unknown. Here, the immune profile of severe COVID-19 was compared with non-SARS-CoV-2 pneumonia ICU patients using longitudinal, high-dimensional single-cell spectral cytometry and algorithm-guided analysis. COVID-19 and non-SARS-CoV-2 pneumonia both showed increased emergency myelopoiesis and displayed features of adaptive immune paralysis. However, pathological immune signatures suggestive of T cell exhaustion were exclusive to COVID-19. The integration of single-cell profiling with a predicted binding capacity of SARS-CoV-2-petides to the patients' HLA profile further linked the COVID-19 immunopathology to impaired virus recognition. Towards clinical translation, circulating NKT cell frequency was identified as a predictive biomarker for patient outcome. The comparative immune map serves to delineate treatment strategies to interfere with the immunopathologic cascade exclusive to severe COVID-19.

Reference

https://www.cell.com/immunity/fulltext/S1074-7613(21)00208-9

SARS-CoV-2 exacerbates proinflammatory responses in myeloid cells through C-type lectin receptors and Tweety family member 2

Abstract

Despite mounting evidence for SARS-CoV-2 engagement with immune cells, most express little, if any, of the canonical receptor of SARS-CoV-2, ACE2. Here, using a myeloid-cell receptor-focused ectopic expression screen, we identified several C-type lectins (DC-SIGN, L-SIGN, LSECtin, ASGR1, and CLEC10A) and Tweety family member 2 (TTYH2) as glycan-dependent binding partners of the SARS-CoV-2 spike. Except for TTYH2, these molecules primarily interacted with spike via regions outside of the receptor-binding domain. Single-cell RNA-sequencing analysis of pulmonary cells

from COVID-19 patients indicated predominant expression of these molecules on myeloid cells. Although these receptors do not support active replication of SARS-CoV-2, their engagement with virus induced robust proinflammatory responses in myeloid cells that correlated with COVID-19 severity. We also generated a bispecific anti-spike nanobody that not only blocked ACE2-mediated infection but also the myeloid receptors-mediated proinflammatory responses. Our findings suggest SARS-CoV-2-myeloid receptor interactions promote immune hyper-activation, which represents potential targets for COVID-19 therapy.

Reference

https://www.cell.com/immunity/fulltext/S1074-7613(21)00212-0

Blood neutrophils from children with COVID-19 exhibit both inflammatory and anti-inflammatory markers

Abstract

Background: Perhaps reflecting that children with COVID-19 rarely exhibit severe respiratory symptoms and often remain asymptomatic, little attention has been paid to explore the immune response in pediatric COVID-19. Here, we analyzed the phenotype and function of circulating neutrophils from children with COVID-19.

Methods: An observational study including 182 children with COVID-19, 21 children with multisystem inflammatory syndrome (MIS-C), and 40 healthy children was performed in Buenos Aires, Argentina. Neutrophil phenotype was analyzed by flow cytometry in blood samples. Cytokine production, plasma levels of IgG antibodies directed to the spike protein of SARS-CoV-2 and citrullinated histone H3 were measured by ELISA. Cell-free DNA was quantified by fluorometry.

Findings: Compared with healthy controls, neutrophils from children with COVID-19 showed a lower expression of CD11b, CD66b, and L-selectin but a higher expression of the activation markers HLA-DR, CD64 and PECAM-1 and the inhibitory receptors LAIR-1 and PD-L1. No differences in the production of cytokines and NETs were observed. Interestingly, the expression of CD64 in neutrophils and the serum concentration of IgG antibodies directed to the spike protein of SARS-CoV-2 distinguished asymptomatic from mild and moderate COVID-19.

Interpretation: Acute lung injury is a prominent feature of severe COVID-19 in adults. A low expression of adhesion molecules together with a high expression of inhibitory receptors in neutrophils from children with COVID-19 might prevent tissue infiltration by neutrophils preserving lung function.

Reference

https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(21)00150-X/fulltext

Publication Date: May 08, 2021

Factors associated with deaths due to COVID-19 versus other causes: Population-based cohort analysis of UK primary care data and linked national death registrations within the OpenSAFELY platform

Abstract

Background: Mortality from COVID-19 shows a strong relationship with age and pre-existing medical conditions, as does mortality from other causes. It was aimed to investigate how specific factors are differentially associated with COVID-19 mortality as compared to mortality from causes other than COVID-19.

Methods: Working on behalf of NHS England, a cohort study was carried out within the OpenSAFELY platform. Primary care data from England were linked to national death registrations. We included all adults (aged ≥18 years) in the database on 1st February 2020 and with >1 year of continuous prior registration; the cut-off date for deaths was 9th November 2020. Associations between individual-level characteristics and COVID-19 and non-COVID deaths, classified according to the presence of a COVID-19 code as the underlying cause of death on the death certificate, were estimated by fitting age- and sex-adjusted logistic models for these two outcomes.

Findings: 17,456,515 Individuals were included. 17,063 died from COVID-19 and 134,316 from other causes. Most factors associated with COVID-19 death were similarly associated with non-COVID death, but the magnitudes of association differed. Older age was more strongly associated with COVID-19 death than non-COVID death (e.g. ORs 40.7 [95% CI 37.7-43.8] and 29.6 [28.9-30.3] respectively for ≥80 vs 50-59 years), as was male sex, deprivation, obesity, and some comorbidities. Smoking, history of cancer and chronic liver disease had stronger associations with non-COVID than

COVID-19 death. All non-white ethnic groups had higher odds than white of COVID-19 death (OR for Black: 2.20 [1.96-2.47], South Asian: 2.33 [2.16-2.52]), but lower odds than white of non-COVID death (Black: 0.88 [0.83-0.94], South Asian: 0.78 [0.75-0.81]).

Interpretation: Similar associations of most individual-level factors with COVID-19 and non-COVID death suggest that COVID-19 largely multiplies existing risks faced by patients, with some notable exceptions. Identifying the unique factors contributing to the excess COVID-19 mortality risk among non-white groups is a priority to inform efforts to reduce deaths from COVID-19.

Reference

https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762(21)00086-7/fulltext

Publication Date: May 07, 2021

Circulating extracellular vesicles are endowed with enhanced procoagulant activity in SARS-CoV-2 infection

Abstract

Background: Coronavirus-2 (SARS-CoV-2) infection causes an acute respiratory syndrome accompanied by multi-organ damage that implicates a prothrombotic state leading to widespread microvascular clots. The causes of such coagulation abnormalities are unknown. The receptor tissue factor, also known as CD142, is often associated with cell-released extracellular vesicles (EV). In this study, we aimed to characterize surface antigens profile of circulating EV in COVID-19 patients and their potential implication as procoagulant agents.

Methods: Serum-derived EV from 67 participants was analyzed who underwent nasopharyngeal swabs molecular test for suspected SARS-CoV-2 infection (34 positives and 33 negatives) and from 16 healthy controls (HC), as referral. A sub-analysis was performed on subjects who developed pneumonia (n = 28). Serum-derived EV were characterized for their surface antigen profile and tested for their procoagulant activity. A validation experiment was performed pre-treating EV with anti-CD142 antibody or with recombinant FVIIa. Serum TNF-α levels were measured by ELISA.

Findings: Profiling of EV antigens revealed a surface marker signature that defines circulating EV in COVID-19. A combination of seven surface molecules (CD49e, CD209, CD86, CD133/1, CD69, CD142, and CD20) clustered COVID (+) versus COVID (-) patients and HC. CD142 showed the highest discriminating performance at both multivariate models and ROC curve analysis. Noteworthy, we found that CD142 exposed onto surface of EV was biologically active. CD142 activity was higher in COVID (+) patients and correlated with TNF-α serum levels.

Interpretation: In SARS-CoV-2 infection the systemic inflammatory response results in cell-release of substantial amounts of procoagulant EV that may act as clotting initiation agents, contributing to disease severity.

Reference

https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(21)00162-6/fulltext

Incorporating false negative tests in epidemiological models for SARS-CoV-2 transmission and reconciling with seroprevalence estimates

Abstract

Susceptible-Exposed-Infected-Removed (SEIR)-type epidemiologic models, modeling unascertained infections latently, can predict unreported cases and deaths assuming perfect testing. We apply a method we developed to account for the high false negative rates of diagnostic RT-PCR tests for detecting an active SARS-CoV-2 infection in a classic SEIR model. The number of unascertained cases and false negatives being unobservable in a real study, population-based serosurveys can help validate model projections. Applying our method to training data from Delhi, India, during March 15–June 30, 2020, we estimate the underreporting factor for cases at 34–53 (deaths: 8–13) on July 10, 2020, largely consistent with the findings of the first round of serosurveys for Delhi (done during June 27–July 10, 2020) with an estimated 22.86% IgG antibody prevalence, yielding estimated underreporting factors of 30–42 for cases. Together, these imply approximately 96–98% cases in Delhi remained unreported (July 10, 2020). Updated calculations using training data during March 15-December 31, 2020 yield estimated underreporting factor for cases at 13–22 (deaths: 3–7) on January 23, 2021, which are again consistent with the latest (fifth) round of serosurveys for Delhi (done during January 15–23, 2021) with an estimated 56.13% IgG antibody prevalence,

yielding an estimated range for the underreporting factor for cases at 17–21. Together, these updated estimates imply approximately 92–96% cases in Delhi remained unreported (January 23, 2021). Such model-based estimates, updated with latest data, provide a viable alternative to repeated resource-intensive serosurveys for tracking unreported cases and deaths and gauging the true extent of the pandemic.

Reference

https://www.nature.com/articles/s41598-021-89127-1

TLR2 senses the SARS-CoV-2 envelope protein to produce inflammatory cytokines

Abstract

The innate immune response is critical for recognizing and controlling infections through the release of cytokines and chemokines. However, severe pathology during some infections, including SARS-CoV-2, is driven by hyperactive cytokine release, or a cytokine storm. The innate sensors that activate production of proinflammatory cytokines and chemokines during COVID-19 remain poorly characterized. In the present study, we show that both TLR2 and MYD88 expression were associated with COVID-19 disease severity. Mechanistically, TLR2 and Myd88 were required for β-coronavirus-induced inflammatory responses, and TLR2-dependent signaling induced the production of proinflammatory cytokines during coronavirus infection independent of viral entry. TLR2 sensed the SARS-CoV-2 envelope protein as its ligand. In addition, blocking TLR2 signaling in vivo provided protection against the pathogenesis of SARS-CoV-2 infection. Overall, our study provides a critical understanding of the molecular mechanism of β-coronavirus sensing and inflammatory cytokine production, which opens new avenues for therapeutic strategies to counteract the ongoing COVID-19 pandemic.

Reference

https://www.nature.com/articles/s41598-021-89127-1

Energetic and structural features of SARS-CoV-2 *N*-protein co-assemblies with nucleic acids

Abstract

Nucleocapsid (N) protein of the SARS-CoV-2 virus packages the viral genome into well-defined ribonucleoprotein particles, but the molecular pathway is still unclear. *N*-Protein is dimeric and consists of two folded domains with nucleic acid (NA) binding sites, surrounded by intrinsically disordered regions that promote liquid-liquid phase separation. Here, biophysical tools were used to study *N*-protein interactions with oligonucleotides of different lengths, examining the size, composition, secondary structure, and energetics of the resulting states. We observe the formation of supramolecular clusters or nuclei preceding growth into phase-separated droplets. Short hexanucleotide NA forms compact 2:2 N-protein/NA complexes with reduced disorder. Longer oligonucleotides expose additional *N*-protein interactions and multi-valent protein-NA interactions, which generate higher-order mixed oligomers and simultaneously promote growth of droplets. Phase separation is accompanied by a significant change in protein secondary structure, different from that caused by initial NA binding, which may contribute to the assembly of ribonucleoprotein particles within macromolecular condensates.

Reference

https://www.cell.com/iscience/fulltext/S2589-0042(21)00491-0

Ultrafast Sample placement on Existing tRees (UShER) enables real-time phylogenetics for the SARS-CoV-2 pandemic

Abstract

As the SARS-CoV-2 virus spreads through human populations, the unprecedented accumulation of viral genome sequences is ushering in a new era of ‘genomic contact tracing’—that is, using viral genomes to trace local transmission dynamics. However, because the viral phylogeny is already so large—and will undoubtedly grow many fold—placing new sequences onto the tree has emerged as a barrier to real-time genomic contact tracing. Here, we resolve this challenge by building an efficient tree-based data structure encoding the inferred evolutionary history of the virus. It was demonstrated

that this approach greatly improves the speed of phylogenetic placement of new samples and data visualization, making it possible to complete the placements under the constraints of real-time contact tracing. Thus, our method addresses an important need for maintaining a fully updated reference phylogeny. These tools were made available to the research community through the University of California Santa Cruz SARS-CoV-2 Genome Browser to enable rapid cross-referencing of information in new virus sequences with an ever-expanding array of molecular and structural biology data. The methods described here will empower research and genomic contact tracing for SARS-CoV-2 specifically for laboratories worldwide.

Reference

https://www.nature.com/articles/s41588-021-00862-7

Non-steroidal anti-inflammatory drug use and outcomes of COVID-19 in the ISARIC Clinical Characterisation Protocol UK cohort: A matched, prospective cohort study

Abstract

Background: Early in the pandemic it was suggested that pre-existing use of non-steroidal anti-inflammatory drugs (NSAIDs) could lead to increased disease severity in patients with COVID-19. NSAIDs are an important analgesic, particularly in those with rheumatological disease, and are widely available to the general public without prescription. Evidence from community studies, administrative data, and small studies of hospitalised patients suggest NSAIDs are not associated with poorer COVID-19 outcomes. We aimed to characterise the safety of NSAIDs and identify whether pre-existing NSAID use was associated with increased severity of COVID-19 disease.

Methods: This prospective, multicentre cohort study included patients of any age admitted to hospital with a confirmed or highly suspected SARS-CoV-2 infection leading to COVID-19 between Jan 17 and Aug 10, 2020. The primary outcome was in-hospital mortality, and secondary outcomes were disease severity at presentation, admission to critical care, receipt of invasive ventilation, receipt of non-invasive ventilation, use of supplementary oxygen, and acute kidney injury. NSAID use was required to be within the 2 weeks before hospital admission. We used logistic regression to estimate the effects of NSAIDs and adjust for confounding variables. We used propensity score

matching to further estimate effects of NSAIDS while accounting for covariate differences in populations.

Results: Between Jan 17 and Aug 10, 2020, we enrolled 78 674 patients across 255 health-care facilities in England, Scotland, and Wales. 72 179 patients had death outcomes available for matching; 40 406 (56·2%) of 71 915 were men, 31 509 (43·8%) were women. In this cohort, 4211 (5·8%) patients were recorded as taking systemic NSAIDs before admission to hospital. Following propensity score matching, balanced groups of NSAIDs users and NSAIDs non-users were obtained (4205 patients in each group). At hospital admission, we observed no significant differences in severity between exposure groups. After adjusting for explanatory variables, NSAID use was not associated with worse in-hospital mortality (matched OR 0·95, 95% CI 0·84–1·07; p=0·35), critical care admission (1·01, 0·87–1·17; p=0·89), requirement for invasive ventilation (0·96, 0·80–1·17; p=0·69), requirement for non-invasive ventilation (1·12, 0·96–1·32; p=0·14), requirement for oxygen (1·00, 0·89–1·12; p=0·97), or occurrence of acute kidney injury (1·08, 0·92–1·26; p=0·33).

Interpretation: NSAID use is not associated with higher mortality or increased severity of COVID-19. Policy makers should consider reviewing issued advice around NSAID prescribing and COVID-19 severity.

Reference

https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(21)00104-1/fulltext

Publication Date: May 06, 2021

Epitope profiling reveals binding signatures of SARS-CoV-2 immune response in natural infection and cross-reactivity with endemic human CoVs

Abstract

A major goal of current severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine efforts is to elicit antibody responses that confer protection. Mapping the epitope targets of the SARS-CoV-2 antibody response is critical for vaccine design, diagnostics, and development of therapeutics. Here, we develop a pan-coronavirus phage display library to map antibody binding sites at high resolution within the complete viral proteomes of all known human-infecting coronaviruses in patients with

mild or moderate/severe coronavirus disease 2019 (COVID-19). It was found that the majority of immune responses to SARS-CoV-2 are targeted to the spike protein, nucleocapsid, and ORF1ab and include sites of mutation in current variants of concern. Some epitopes are identified in the majority of samples, while others are rare, and we find variation in the number of epitopes targeted between individuals. Low levels of SARS-CoV-2 cross-reactivity in individuals were found with no exposure to the virus and significant cross-reactivity with endemic human coronaviruses (CoVs) in convalescent sera from patients with COVID-19.

Reference

https://www.cell.com/cell-reports/fulltext/S2211-1247(21)00506-4

Profiling B cell immunodominance after SARS-CoV-2 infection reveals antibody evolution to non-neutralizing viral targets

Abstract

Dissecting the evolution of memory B cells (MBCs) against SARS-CoV-2 is critical for understanding antibody recall upon secondary exposure. Here, single-cell sequencing were used to profile SARS-CoV-2-reactive B cells in 38 COVID-19 patients. Using oligo-tagged antigen baits, we isolated B cells specific to the SARS-CoV-2 spike, nucleoprotein (NP), open reading frame 8 (ORF8), and endemic human coronavirus (HCoV) spike proteins. SARS-CoV-2 spike-specific cells were enriched in the memory compartment of acutely infected and convalescent patients several months post symptom onset. With severe acute infection, substantial populations of endemic HCoV-reactive antibody-secreting cells were identified and possessed highly mutated variable genes, signifying preexisting immunity. Finally, MBCs exhibited pronounced maturation to NP and ORF8 over time, especially in older patients. Monoclonal antibodies against these targets were non-neutralizing and non-protective *in vivo*. These findings reveal antibody adaptation to non-neutralizing intracellular antigens during infection, emphasizing the importance of vaccination for inducing neutralizing spike-specific MBCs.

Reference

https://www.cell.com/immunity/fulltext/S1074-7613(21)00198-9

Comparative immune profiling of acute respiratory distress syndrome patients with or without SARS-CoV2 infection

Abstract

Acute respiratory distress syndrome (ARDS) is the main complication of COVID-19, requiring admission to Intensive Care Unit (ICU). Despite extensive immune profiling of COVID-19 patients, to what extent COVID-19-associated ARDS differs from other causes of ARDS remains unknown. To address this question, we build 3 cohorts of patients categorize in COVID-19negARDSpos, COVID-19posARDSpos, and COVID-19posARDSneg, and compare their immune landscape analyze by high-dimensional mass cytometry on peripheral blood. A cell signature associating S100A9/calprotectin-producing CD169pos monocytes, plasmablasts, and Th1 cells is found in COVID-19posARDSpos, unlike COVID-19negARDSpos patients. Moreover, this signature is essentially share with COVID-19posARDSneg patients, suggesting that severe COVID-19 patients, whatever they experience or not ARDS, display similar immune profiles. We show an increase in CD14posHLA-DRlow and CD14lowCD16pos monocytes correlate to the occurrence of adverse events during ICU stay. It was demonstrated that COVID-19-associated ARDS display a specific immune profile, and might benefit from personalize therapy in addition to standard ARDS management.

Reference

https://www.cell.com/cell-reports-medicine/fulltext/S2666-3791(21)00119-1

Association between ACE2 and TMPRSS2 nasopharyngeal expression and COVID-19 respiratory distress

Abstract

ACE2 and TMPRSS2 are key players on SARS-CoV-2 entry into host cells. However, it is still unclear whether expression levels of these factors could reflect disease severity. Here, a case–control study was conducted with 213 SARS-CoV-2 positive individuals where cases were defined as COVID-19 patients with respiratory distress requiring oxygen support (N = 38) and controls were those with mild to moderate symptoms of the disease who did not need oxygen therapy along the entire clinical course (N = 175). ACE2 and TMPRSS2 mRNA levels were evaluated in nasopharyngeal swab samples

by RT-qPCR and logistic regression analyzes were applied to estimate associations with respiratory outcomes. ACE2 and TMPRSS2 levels positively correlated with age, which was also strongly associated with respiratory distress. Increased nasopharyngeal ACE2 levels showed a protective effect against this outcome (adjOR = 0.30; 95% CI 0.09–0.91), while TMPRSS2/ACE2 ratio was associated with risk (adjOR = 4.28; 95% CI 1.36–13.48). On stepwise regression, TMPRSS2/ACE2 ratio outperformed ACE2 to model COVID-19 severity. When nasopharyngeal swabs were compared to bronchoalveolar lavages in an independent cohort of COVID-19 patients under mechanical ventilation, similar expression levels of these genes were observed. These data suggest nasopharyngeal TMPRSS2/ACE2 as a promising candidate for further prediction models on COVID-19.

Reference

https://www.nature.com/articles/s41598-021-88944-8

Dynamic and features of SARS-CoV-2 infection in Gabon

Abstract

In a context where SARS-CoV-2 population-wide testing is implemented, clinical features and antibody response in those infected have never been documented in Africa. Yet, the information provided by analyzing data from population-wide testing is critical to understand the infection dynamics and devise control strategies. We described clinical features and assessed antibody response in people screened for SARS-CoV-2 infection. We analyzed data from a cohort of 3464 people that we molecularly screened for SARS-CoV-2 infection in our routine activity. We recorded people SARS-CoV-2 diagnosis, age, gender, blood types, white blood cells (WBC), symptoms, chronic disease status and time to SARS-CoV-2 RT-PCR conversion from positive to negative. The age-based distribution of SARS-CoV-2 infection was calculated, analyzed the proportion and the spectrum of COVID-19 severity. Furthermore, in a nested sub-study, we screened 83 COVID-19 patients and 319 contact-cases for anti-SARS-CoV-2 antibodies. Males and females accounted for respectively 51% and 49% of people screened. The studied population median and mean age were both 39 years. 592 out of 3464 people (17.2%) were diagnosed with SARS-CoV-2 infection with males and females representing, respectively, 53% and

47%. The median and mean ages of SARS-CoV-2 infected subjects were 37 and 38 years respectively. The lowest rate of infection (8%) was observed in the elderly (aged > 60). The rate of SARS-Cov-2 infection in both young (18–35 years old) and middle-aged adults (36–60 years old) was around 20%. The analysis of SARS-CoV-2 infection age distribution showed that middle-aged adults accounted for 54.7% of SARS-CoV-2 positive persons, followed respectively by young adults (33.7%), children (7.7%) and elderly (3.8%). 68% (N = 402) of SARS-CoV-2 infected persons were asymptomatic, 26.3% (N = 156) had influenza-like symptoms, 2.7% (N = 16) had influenza-like symptoms associated with anosmia and ageusia, 2% (N = 11) had dyspnea and 1% (N = 7) had respiratory failure, which resulted in death. Data also showed that 12% of SARS-CoV-2 infected subjects, had chronic diseases. Hypertension, diabetes, and asthma were the top concurrent chronic diseases representing respectively 58%, 25% and 12% of recorded chronic diseases. Half of SARS-CoV-2 RT-PCR positive patients were cured within 14 days following the initiation of the anti-COVID-19 treatment protocol. 78.3% of COVID-19 patients and 55% of SARS-CoV-2 RT-PCR confirmed negative contact-cases were positive for anti-SARS-CoV-2 antibodies. Patients with severe-to-critical illness have higher leukocytes, higher neutrophils and lower lymphocyte counts contrarily to asymptomatic patients and patients with mild-to-moderate illness. Neutrophilic leukopenia was more prevalent in asymptomatic patients and patients with mild-to-moderate disease for 4 weeks after diagnosis (27.1–42.1%). In Patients with severe-to-critical illness, neutrophilic leukocytosis or neutrophilia (35.6–50%) and lymphocytopenia (20–40%) were more frequent. More than 60% of participants were blood type O. It is also important to note that infection rate was slightly higher among A and B blood types compared with type O. In this African setting, young and middle-aged adults are most likely driving community transmission of COVID-19. The rate of critical disease is relatively low. The high rate of anti-SARS-CoV-2 antibodies observed in SARS-CoV-2 RT-PCR negative contact cases suggests that subclinical infection may have been overlooked in the setting.

Reference

https://www.nature.com/articles/s41598-021-87043-y

Type I and III interferon responses in SARS-CoV-2 infection

Abstract

Coronavirus disease 2019 (COVID-19), the current pandemic disease, is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Type I and III interferons (IFNs) are innate cytokines that are important in the first-line defense against viruses. Similar to many other viruses, SARS-CoV-2 has evolved mechanisms for evading the antiviral effects of type I and III IFNs at multiple levels, including the induction of IFN expression and cellular responses to IFNs. In this review, the innate sensing mechanisms of SARS-CoV-2 and the mechanisms used by SARS-CoV-2 to evade type I and III IFN responses were described. It was also discussed that contradictory reports regarding impaired and robust type I IFN responses in patients with severe COVID-19. Finally, it was also discussed, how delayed but exaggerated type I IFN responses can exacerbate inflammation and contribute to the severe progression of COVID-19.

Reference

https://www.nature.com/articles/s12276-021-00592-0

Seroprevalence of SARS-CoV-2 IgG antibodies and risk factors in health care workers at an academic medical center in Boston, Massachusetts

Abstract

Healthcare workers (HCWs) are at an increased risk of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a novel virus that causes Coronavirus Disease (COVID-19). It was aimed to assess the seroprevalence of SARS-CoV-2 IgG among healthcare workers and compare risk-factors between seropositive and seronegative HCWs. In this observational study, serum samples were collected from HCWs between July 13th to 26th, 2020 at Boston Medical Center (BMC). Samples were subsequently tested for SARS-CoV-2 IgG antibody using the Abbott SARS-CoV-2 IgG assay. Participants also answered a questionnaire capturing data on demographics, history of COVID-19 symptoms, occupation, infection prevention and control measures. Overall, 95 of 1743 (5.5%) participants tested positive for SARS-CoV-2 IgG. Of these, 1.8% of the participants had mild or no COVID-19 symptoms and did not require a diagnostic

test. Seropositivity was not associated with gender, occupation, hand hygiene and personal protective equipment (PPE) practices amongst HCWs. However, lack of physical distancing among health care workers in work areas and break room was associated with seropositivity ($p = 0.05$, $p = 0.003$, respectively). The majority of the HCWs are negative for SARS-CoV-2 IgG. This data highlights the need to promote infection prevention measures, and the importance of distance amongst co-workers to help mitigate infection rates.

Reference

https://www.nature.com/articles/s41598-021-89107-5

Rapid development of neutralizing and diagnostic SARS-COV-2 mouse monoclonal antibodies

Abstract

The need for high-affinity, SARS-CoV-2-specific monoclonal antibodies (mAbs) is critical in the face of the global COVID-19 pandemic, as such reagents can have important diagnostic, research, and therapeutic applications. Of greatest interest is the ~ 300 amino acid receptor binding domain (RBD) within the S1 subunit of the spike protein because of its key interaction with the human angiotensin converting enzyme 2 (hACE2) receptor present on many cell types, especially lung epithelial cells. Here, the development and functional characterization of 29 nM-affinity mouse SARS-CoV-2 mAbs was reported and created by an accelerated immunization and hybridoma screening process. Differing functions, including binding of diverse protein epitopes, viral neutralization, impact on RBD-hACE2 binding, and immunohistochemical staining of infected lung tissue, were correlated with variable gene usage and sequence.

Reference

https://www.nature.com/articles/s41598-021-88809-0

The COVID-19 puzzle: Deciphering pathophysiology and phenotypes of a new disease entity

Abstract

The zoonotic SARS-CoV-2 virus that causes COVID-19 continues to spread worldwide, with devastating consequences. While the medical community has gained insight into

the epidemiology of COVID-19, important questions remain about the clinical complexities and underlying mechanisms of disease phenotypes. Severe COVID-19 most commonly involves respiratory manifestations, although other systems are also affected, and acute disease is often followed by protracted complications. Such complex manifestations suggest that SARS-CoV-2 dysregulates the host response, triggering wide-ranging immuno-inflammatory, thrombotic, and parenchymal derangements. The intricacies of COVID-19 pathophysiology were reviewed, its various phenotypes, and the anti-SARS-CoV-2 host response at the humoral and cellular levels. Some similarities exist between COVID-19 and respiratory failure of other origins, but evidence for many distinctive mechanistic features indicates that COVID-19 constitutes a new disease entity, with emerging data suggesting involvement of an endotheliopathy-centred pathophysiology. Further research, combining basic and clinical studies, is needed to advance understanding of pathophysiological mechanisms and to characterise immuno-inflammatory derangements across the range of phenotypes to enable optimum care for patients with COVID-19.

Reference

https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00218-6/fulltext

CORRESPONDANCE

Publication Date: Apr 12, 2021

Data discrepancies and substandard reporting of interim data of Sputnik V phase 3 trial

Restricted access to data hampers trust in research. Access to data underpinning study findings is imperative to check and confirm the findings claimed. It is even more serious if there are apparent errors and numerical inconsistencies in the statistics and results presented. Regrettably, this seems to be what is happening in the case of the Sputnik V phase 3 trial.

Several experts found problematic data in the published phase 1/2 results. Multiple independent requests were made for access to the raw dataset, but these were never answered. Despite publicly denying some problems, formal corrections were made to the Article, thus addressing some concerns. Notwithstanding the previous issues and lack of transparency, the interim results from the phase 3 trial of the Sputnik V vaccine again raise serious concerns. For more details, read the link given below.

Reference

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00899-0/fulltext

Heterologous prime-boost COVID-19 vaccination: Initial reactogenicity data

There is significant international interest in heterologous prime-boost COVID-19 vaccination to mitigate against supply shocks or shortages that might otherwise reduce the speed of vaccine roll-out. Additionally, in light of changing recommendations regarding use of the ChAdOx1 nCoV-19 (ChAd) COVID-19 vaccine (Vaxzevria, AstraZeneca), several countries are now advising that individuals previously primed with this vaccine should now receive an alternative vaccine as their second dose, most commonly mRNA vaccines such as the BNT162b2 (BNT) COVID-19 vaccine (Comirnaty, Pfizer-BioNTech), administered in a heterologous prime-boost schedule. To date there are no data on the immunogenicity, reactogenicity, or safety of such schedules. Com-COV (ISRCTN 69254139) is a UK multi-centre, participant-masked, randomised heterologous prime-boost COVID-19 vaccination study comparing all four

prime-boost permutations of the ChAd and BNT vaccines both at 28-day and 84-day prime-boost intervals. Participants are 50 years and older with no or mild-to-moderate, well controlled comorbidity and were recruited across eight sites. The protocol is available online. Following consultation with the study trial steering committee, here we present the initial reactogenicity and safety data, ahead of the primary immunological outcome, which is projected to be available in June, 2021. Reactogenicity data presented here consist of self-reported solicited local and systemic symptoms collected in the 7 days after both prime and boost vaccination in participants randomised to receive vaccines at 28-day intervals. Haematology and biochemistry safety monitoring blood results are also reported from the immunology cohort (100 participants with additional visits), at baseline (before the prime dose), at day 28 (before the boost dose) and 7 days post-boost, graded according to a modified US Food and Drug Administration toxicity scale (appendix). All analyses are descriptive, as the study was not powered for reactogenicity, with endpoints reported as frequencies and percentages, together with absolute differences between heterologous and homologous vaccine schedules and corresponding 95% CIs. For more details, read the given link below.

Reference

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)01115-6/fulltext

COMMENT

Publication Date: May 12, 2021

HERV-W Envelope expression in blood leukocytes as a marker of disease severity of COVID-19

It is the midst of a pandemic, caused by SARS-CoV-2, that has shaken the entire social and economic fabric of society. Within less than a year it spread across the entire globe and has spared no country, society, race or age group. Even several world leaders have been infected. While, a great progress was made towards developing effective vaccines, to date we do not have any effective anti-viral agents. This desperate situation has called for desperate measures. For example, hydroxychloroquine was initially used for treating the infection based on minimal in vitro data, resulting in world-wide shortages of the drug, only for subsequent clinical trials to show that it was ineffective in treating the infection. It has become clear however, that in the early phases of the infection particularly in hospitalized patients, anti-inflammatory measures such as the use of corticosteroids can be helpful. All the same, potent immunosuppression can be detrimental to the host since this is what is necessary for the ultimate recovery of the patient. Hence better methods are necessary that would modulate the immune system more precisely to prevent organ damage and yet preserve the antiviral effects. The current study by Balestrieri et al. in *EBioMedicine*, studied 30 hospitalized patients infected with SARS-CoV-2 with a wide range of severity of illnesses. They were classified as asymptomatic, presymptomatic, mild, moderate or severe. 24/30 patients were males. They determined the expression of the envelope protein of an endogenous retrovirus family W (HERV-W), in blood leukocytes and compared it to other immune markers and the clinical status of the individuals. The expression of HERV-W envelope protein has been previously implicated in certain autoimmune diseases, such as multiple sclerosis (MS), chronic inflammatory demyelinating polyneuropathy and type-1 diabetes. Increased levels of HERV-W transcripts have also been found in schizophrenia and bipolar disorder. For more details, read the given link below.

Reference

https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(21)00156-0/fulltext

Applying prospective genomic surveillance to support investigation of hospital-onset COVID-19

Here, an update on our previous article was provided, which described the use of rapid SARS-CoV-2 genome sequencing to investigate hospital-acquired infections (HAIs) at Cambridge University Hospitals NHS Foundation Trust (CUH), Cambridge, UK. CUH experienced a substantial second wave of COVID-19 (figure). Between Nov 2, 2020, and Feb 7, 2021, 162 (14%) of 1178 patients with COVID-19 at CUH had a suspected or definite HAI (as previously defined1), and 465 infected health-care workers (HCWs) were identified *via* the staff screening programme. Nanopore sequencing was attempted for 513 (44%) of 1178 patients, prioritising those with hospital-onset infections, and 324 (70%) of 465 HCWs; 252 (21%) of 1178 patients and 317 (68%) of 465 HCWs had SARS-CoV-2 genomes available after quality control filtering (as previously described1). Patient coverage was lower than in the previous study and for HCWs, reflecting different diagnostic testing methods and limitations on sequencing capacity. The frequency of the B.1.1.7 PANGO-lineage increased from 8% (nine of 109) in November, 2020, to 83% (257 of 311) in January, 2021. As in the first wave, outbreaks of hospital-onset COVID-19 occurred on wards intended for patients without COVID-19, termed green wards. Where genomics were available, cases on these wards were often phylogenetically clustered (virus genomes with zero to one single nucleotide polymorphism differences), consistent with ward-based transmission. This transmission occurred despite substantial efforts to reduce HAIs, including universal surgical mask wearing by staff, SARS-CoV-2 screening of all patients at hospital admission and regularly thereafter, cohorting of patients to green, amber, and red wards, and a comprehensive staff screening programme. Continued hospital-based transmission despite these efforts emphasises how challenging it is to limit SARS-CoV-2 transmission in hospitals with limited side-room capacity, given the high infectivity of SARS-CoV-2 and potential for asymptomatic transmission. Genomic data were presented at seven of 11 clinical HAI review meetings and at infection-control meetings, informing decision-making. Staff vaccinations began in January, 2021, and have already had a substantial impact on reducing COVID-19 incidence. For more details, read the given link below.

Reference

https://www.nature.com/articles/s41577-021-00553-8

Publication Date: May 06, 2021

Aerosol generating procedures: are they of relevance for transmission of SARS-CoV-2?

It is now generally accepted that SARS-CoV-2 can be spread by aerosols as well as larger droplets from the upper respiratory tract, although the relative importance of aerosol transmission remains incompletely answered. Despite this, current UK infection control guidance for hospitals is centred on the premise that aerosols are only generated by specific medical interventions designated as aerosol generating procedures (AGPs). This draws from epidemiological observations during the 2003 outbreak of severe acute respiratory syndrome, during which certain procedures appeared to be associated with an increased risk of staff infection (particularly tracheal intubation), and these procedures had a theoretical risk of viral aerosolisation. However, the evidence supporting aerosolisation during these procedures was, before the pandemic, remarkably slim, with aerosolisation being assumed on the basis of the precautionary principle and low quality mechanistic studies. This view of aerosol generation subsequently led to a dichotomisation—later codified in international guidance—that categorised all medical activities into either AGPs, where potentially infectious aerosols are generated, versus everything else, where the risk of potentially infectious aerosol is presumed to be negligible. The logical extension of this dichotomy has resulted in health-care workers in many countries undertaking interventions classified as AGPs wearing higher levels of personal protective equipment (PPE), such as FFP3 or N95 masks, whereas those health-care workers providing other medical care have not been afforded the same protection, as infectious aerosol is not considered a risk outside of AGPs. For more details, read the given link below.

Reference

https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00216-2/fulltext

REPORT

Publication Date: May 11, 2021

SARS-CoV-2 targets glial cells in human cortical organoids

Coronavirus disease 2019 (COVID-19) patients have manifested a variety of neurological complications, and there is still much to reveal regarding the neurotropism of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Human stem cell-derived brain organoids offer a valuable in vitro approach to study the cellular effects of SARS-CoV-2 on the brain. Here we used human embryonic stem cell-derived cortical organoids to investigate whether SARS-CoV-2 could infect brain tissue in vitro and found that cortical organoids could be infected at low viral titers and within 6 h. Importantly, we show that glial cells and cells of the choroid plexus were preferentially targeted in our model, but not neurons. Interestingly, we also found expression of angiotensin-converting enzyme 2 in SARS-CoV-2 infected cells; however, viral replication and cell death involving DNA fragmentation does not occur. We believe that our model is a tractable platform to study the cellular effects of SARS-CoV-2 infection in brain tissue.

Reference

https://www.cell.com/stem-cell-reports/fulltext/S2213-6711(21)00046-1