

COVID-19

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RESEARCH PUBLICATIONS

Publication Date: Jan 27, 2021

Integrating deep learning CT-scan model, biological and clinical variables to predict severity of COVID-19 patients

Abstract

The SARS-COV-2 pandemic has put pressure on intensive care units, so that identifying predictors of disease severity is a priority. 58 Clinical and biological variables, and chest CT scan data were collected, from 1003 coronavirus-infected patients from two French hospitals. A deep learning model was trained based on CT scans to predict severity. The multimodal AI-severity score was constructed that includes 5 clinical and biological variables (age, sex, oxygenation, urea, platelet) in addition to the deep learning model. It was shown that neural network analysis of CT-scans brings unique prognosis information, although it is correlated with other markers of severity (oxygenation, LDH, and CRP) explaining the measurable but limited 0.03 increase of AUC obtained when adding CT-scan information to clinical variables. Here, it was shown that when comparing AI-severity with 11 existing severity scores, we find significantly improved prognosis performance; AI-severity can therefore rapidly become a reference scoring approach.

Reference

<https://www.nature.com/articles/s41467-020-20657-4>

Impact of the SARS-CoV-2 pandemic and associated lockdown measures on attendances at emergency departments in English hospitals: A retrospective database study

Abstract

Background: The SARS-CoV-2 outbreak and associated lockdown measures have challenged healthcare. It was examined that how attendances to ED in England were impacted.

Methods: Interrupted time series regression (January 2019 to June 2020) of data from EDs in 41 English NHS Trusts was used to estimate the initial decrease in attendances and the rate of increase following an interruption from 11 March – 7 April 2020, which included the 23 March lockdown in England.

Findings: The SARS-CoV-2 interruption led to an initial 51.1% reduction (95% CI 46.3–55.9%) in ED attendances followed by a linear increase in attendances of 3.0% per week (95% CI 2.5–3.5%). Significantly larger initial reductions were seen in those aged 0–19 years (69.1%), Indian (64.9%), Pakistani (71.8%), Bangladeshi (75.3%), African (63.5%) and Chinese people (74.5%), self-conveying attendees (60.3%) and those presenting with contusions or abrasions (66.9%), muscle and tendon injuries (65.6%), and those with a diagnosis that was not classifiable (72.7%). Significantly smaller initial reductions were seen in those aged 65–74 years (42.6%), 75+ years (40.1%), those conveyed by ambulance (31.9%), and those presenting with the following conditions: central nervous system (44.9%), haematological (44.0%), cardiac (43.7%), gastrointestinal (43.4%), gynaecological (43.2%), psychiatric (40.4%), poisoning (39.7%), cerebro-vascular (39.0%), endocrinological (36.1%), other vascular (34.6%), and maxillo-facial (19.7%). No significant differences in the initial reduction of activity were seen in subgroups defined by sex, deprivation, urbanicity or acuity.

Interpretation: The SARS-CoV-2 outbreak and lockdown substantially reduced ED activity. The reduction varied by age groups, ethnicity, arrival mode and diagnostic group but not by sex, deprivation, urbanicity or acuity.

Reference

[https://www.thelancet.com/journals/lanepi/article/PIIS2666-7762\(21\)00011-9/fulltext](https://www.thelancet.com/journals/lanepi/article/PIIS2666-7762(21)00011-9/fulltext)

Toward effective government communication strategies in the era of COVID-19

Abstract

Several countries have successfully reduced their COVID-19 infection rate early, while others have been overwhelmed. The reasons for the differences are complex, but response efficacy has in part depended on the speed and scale of governmental intervention and how communities have received, perceived, and acted on the information provided by governments and other agencies. While there is no 'one size fits all' communications strategy to deliver information during a prolonged crisis, in this article, key findings were drawn from scholarship in multiple social science disciplines to highlight some fundamental characteristics of effective governmental crisis communication. We then present ten recommendations for effective communication strategies to engender maximum support and participation. It was argued that an effective communication strategy is a two-way process that involves clear messages, delivered via appropriate platforms, tailored for diverse audiences, and shared by trusted people. Ultimately, the long-term success depends on developing and maintaining public trust. It was outlined how government policymakers can engender widespread public support and participation through increased and ongoing community engagement. It was argued that a diversity of community groups must be included in engagement activities. It was also highlighted the implications of emerging digital technologies in communication and engagement activities.

Reference

<https://www.nature.com/articles/s41599-020-00701-w>

Altered high-density lipoprotein composition and functions during severe COVID-19

Abstract

Coronavirus disease 2019 (COVID-19) pandemic is affecting millions of patients worldwide. The consequences of initial exposure to SARS-CoV-2 go beyond pulmonary damage, with a particular impact on lipid metabolism. Decreased levels in HDL-C were reported in COVID-19 patients. Since HDL particles display antioxidant, anti-inflammatory and potential anti-infectious properties, we aimed at characterizing HDL

proteome and functionality during COVID-19 relative to healthy subjects. HDLs were isolated from plasma of 8 severe COVID-19 patients sampled at admission to intensive care unit (Day 1, D1) at D3 and D7, and from 16 sex- and age-matched healthy subjects. Proteomic analysis was performed by LC-MS/MS. The relative amounts of proteins identified in HDLs were compared between COVID-19 and controls. apolipoprotein A-I and paraoxonase 1 were confirmed by Western-blot analysis to be less abundant in COVID-19 versus controls, whereas serum amyloid A and alpha-1 antitrypsin were higher. HDLs from patients were less protective in endothelial cells stimulated by TNF α (permeability, VE-cadherin disorganization and apoptosis). In these conditions, HDL inhibition of apoptosis was blunted in COVID-19 relative to controls. In conclusion, we show major changes in HDL proteome and decreased functionality in severe COVID-19 patients.

Reference

<https://www.nature.com/articles/s41598-021-81638-1>

Identification of SARS-CoV-2 spike mutations that attenuate monoclonal and serum antibody neutralization

Abstract

Neutralizing antibodies against the SARS-CoV-2 spike (S) protein are a goal of COVID-19 vaccines and have received emergency use authorization as therapeutics. However, viral escape mutants could compromise efficacy. To define immune-selected mutations in the S protein, we exposed a VSV-eGFP-SARS-CoV-2-S chimeric virus, in which the VSV glycoprotein is replaced with the S protein, to 19 neutralizing monoclonal antibodies (mAbs) against the receptor-binding domain (RBD) and generated 50 different escape mutants. Each mAb had a unique resistance profile, although many shared residues within an epitope of the RBD. Some variants (e.g., S477N) were resistant to neutralization by multiple mAbs, whereas others (e.g., E484K) escaped neutralization by convalescent sera. Additionally, sequential selection identified mutants that escape neutralization by antibody cocktails. Comparing these antibody-mediated mutations with sequence variation in circulating SARS-CoV-2 revealed substitutions that may attenuate neutralizing immune responses in some humans and thus warrant further investigation.

Reference

[https://www.cell.com/cell-host-microbe/fulltext/S1931-3128\(21\)00044-5](https://www.cell.com/cell-host-microbe/fulltext/S1931-3128(21)00044-5)

Mutational signatures and heterogeneous host response revealed *via* large-scale characterization of SARS-CoV-2 genomic diversity

Abstract

To dissect the mechanisms underlying the inflation of variants in the SARS-CoV-2 genome, we present a large-scale analysis of intra-host genomic diversity, which reveals that most samples exhibit heterogeneous genomic architectures, due to the interplay between host-related mutational processes and transmission dynamics. The decomposition of minor variants profiles unveils three non-overlapping mutational signatures related to nucleotide substitutions and likely ruled by APOBEC, Reactive Oxygen Species and ADAR, highlighting heterogeneous host responses to SARS-CoV-2 infections. A corrected-for-signatures dN/dS analysis demonstrates that such mutational processes are affected by purifying selection, with important exceptions. In fact, several mutations appear to transit toward clonality, defining new clonal genotypes that increase the overall genomic diversity. Furthermore, the phylogenomic analysis shows the presence of homoplasies and supports the hypothesis of transmission of minor variants. This study paves the way for the integrated analysis of intra-host genomic diversity and clinical outcome of SARS-CoV-2 infections.

Reference

[https://www.cell.com/iscience/fulltext/S2589-0042\(21\)00084-5](https://www.cell.com/iscience/fulltext/S2589-0042(21)00084-5)

Predictors of negative first SARS-CoV-2 RT-PCR despite final diagnosis of COVID-19 and association with outcome

Abstract

Reverse transcriptase-polymerase chain reaction (RT-PCR) testing is an important tool for diagnosing coronavirus disease 2019 (COVID-19). However, performance concerns have emerged recently, notably regarding sensitivity. It was hypothesized that the clinical, biological, and radiological characteristics of patients with a false-negative first RT-PCR test and a final diagnosis of COVID-19 might differ from those of patients with a positive first RT-PCR test. It was conducted a multicenter matched case–control study

in COVID-19 patients. Patients with a negative first RT-PCR test were matched to patients with a positive first RT-PCR test on age, sex, and initial admission unit (ward or intensive care). It was included 80 cases and 80 controls between March 30, and June 22, 2020. Neither mortality at hospital discharge nor hospital stay length differed between the two groups ($P = 0.80$ and $P = 0.54$, respectively). By multivariate analysis, two factors were independently associated with a lower risk of a first false-negative test, namely, headache (adjusted OR [aOR], 0.07; 95% confidence interval [95% CI], 0.01–0.49; $P = 0.007$) and fatigue/malaise (aOR, 0.16; 95% CI, 0.03–0.81; $P = 0.027$); two other factors were independently associated with a higher risk of a first false-negative test, namely, platelets $> 207 \cdot 10^3 \text{ mm}^{-3}$ (aOR, 3.81; 95% CI, 1.10–13.16; $P = 0.034$) and C-reactive protein $> 79.8 \text{ mg} \cdot \text{L}^{-1}$ (aOR, 4.00; 95% CI, 1.21–13.19; $P = 0.023$). Patients with suspected COVID-19 whose laboratory tests indicating marked inflammation were at higher risk of a first false-negative RT-PCR test. Strategies involving serial RT-PCR testing must be rigorously evaluated.

Reference

<https://www.nature.com/articles/s41598-021-82192-6>

Potential discharge, attenuation and exposure risk of SARS-CoV-2 in natural water bodies receiving treated wastewater

Abstract

Recently reported detection of SARS-CoV-2 in wastewater around the world has led to emerging concerns on potential risk in water bodies receiving treated wastewater effluent. This review aims to provide an up-to-date state of key knowledge on the impact of SARS-CoV-2 in natural water bodies receiving treated wastewater. In this review, SARS-CoV-2 concentrations in wastewater, expected removal in WWTPs, and possible dilution and decay in water bodies are reviewed based on past studies on SARS-CoV-2 and related enveloped viruses. It was suggested that a quantitative microbial risk assessment (QMRA) framework to estimate the potential risk of SARS-CoV-2 in natural water bodies through various water activities. Dose–response model of SARS-CoV and Poisson’s distribution is employed to estimate possible viral ingestion and the annual chance of infection through several water activities in natural water bodies. Finally, future perspectives and research needs have been addressed to overcome the

limitations and uncertainty in the risk assessment of SARS-CoV-2 in natural water bodies.

Reference

<https://www.nature.com/articles/s41598-021-82192-6>

Cryo-EM structures of the SARS-CoV-2 endoribonuclease Nsp15 reveal insight into nuclease specificity and dynamics

Abstract

Nsp15, a uridine specific endoribonuclease conserved across coronaviruses, processes viral RNA to evade detection by host defense systems. Crystal structures of Nsp15 from different coronaviruses have shown a common hexameric assembly, yet how the enzyme recognizes and processes RNA remains poorly understood. Here a series of cryo-EM reconstructions of SARS-CoV-2 Nsp15 was reported, in both apo and UTP-bound states. The cryo-EM reconstructions, combined with biochemistry, mass spectrometry, and molecular dynamics, expose molecular details of how critical active site residues recognize uridine and facilitate catalysis of the phosphodiester bond. Mass spectrometry revealed the accumulation of cyclic phosphate cleavage products, while analysis of the apo and UTP-bound datasets revealed conformational dynamics not observed by crystal structures that are likely important to facilitate substrate recognition and regulate nuclease activity. Collectively, these findings advance understanding of how Nsp15 processes viral RNA and provide a structural framework for the development of new therapeutics.

Reference

<https://www.nature.com/articles/s41467-020-20608-z>

Elucidating the tunability of binding behavior for the MERS-CoV macro domain with NAD metabolites

Abstract

The macro domain is an ADP-ribose (ADPR) binding module, which is considered to act as a sensor to recognize nicotinamide adenine dinucleotide (NAD) metabolites, including poly ADPR (PAR) and other small molecules. The recognition of macro

domains with various ligands is important for a variety of biological functions involved in NAD metabolism, including DNA repair, chromatin remodeling, maintenance of genomic stability, and response to viral infection. Nevertheless, how the macro domain binds to moieties with such structural obstacles using a simple cleft remains a puzzle. We systematically investigated the Middle East respiratory syndrome-coronavirus (MERS-CoV) macro domain for its ligand selectivity and binding properties by structural and biophysical approaches. Of interest, NAD, which is considered not to interact with macro domains, was co-crystallized with the MERS-CoV macro domain. Further studies at physiological temperature revealed that NAD has similar binding ability with ADPR because of the accommodation of the thermal-tunable binding pocket. This study provides the biochemical and structural bases of the detailed ligand-binding mode of the MERS-CoV macro domain. In addition, our observation of enhanced binding affinity of the MERS-CoV macro domain to NAD at physiological temperature highlights the need for further study to reveal the biological functions.

Reference

<https://www.nature.com/articles/s42003-020-01633-6>

A PCR amplicon-based SARS-CoV-2 replicon for antiviral evaluation

Abstract

The development of specific antiviral compounds to SARS-CoV-2 is an urgent task. One of the obstacles for the antiviral development is the requirement of biocontainment because infectious SARS-CoV-2 must be handled in a biosafety level-3 laboratory. Replicon, a non-infectious self-replicative viral RNA, could be a safe and effective tool for antiviral evaluation. Herein, a PCR-based SARS-CoV-2 replicon was generated. Eight fragments covering the entire SARS-CoV-2 genome except S, E, and M genes were amplified with HiBiT-tag sequence by PCR. The amplicons were ligated and in vitro transcribed to RNA. The cells electroporated with the replicon RNA showed more than 3000 times higher luminescence than MOCK control cells at 24 h post-electroporation, indicating robust translation and RNA replication of the replicon. The replication was drastically inhibited by remdesivir, an RNA polymerase inhibitor for SARS-CoV-2. The IC_{50} of remdesivir in this study was 0.29 μ M, generally consistent to the IC_{50} obtained using infectious SARS-CoV-2 in a previous study (0.77 μ M). Taken

together, this system could be applied to the safe and effective antiviral evaluation without using infectious SARS-CoV-2. Because this is a PCR-based and transient replicon system, further improvement including the establishment of stable cell line must be achieved.

Reference

<https://www.nature.com/articles/s41598-021-82055-0>

Publication Date: Jan 26, 2021

Overcoming limitations in the availability of swabs systems used for SARS-CoV-2 laboratory diagnostics

Abstract

The diagnosis of COVID-19 relies on the direct detection of SARS-CoV-2 RNA in respiratory specimens by RT-PCR. The pandemic spread of the disease caused an imbalance between demand and supply of materials and reagents needed for diagnostic purposes including swab sets. In a comparative effectiveness study, it was conducted serial follow-up swabs in hospitalized laboratory-confirmed COVID-19 patients. It was assessed that the diagnostic performance of an in-house system developed according to recommendations by the US CDC. In a total of 96 serial swabs, we found significant differences in the accuracy of the different swab systems to generate a positive result in SARS-CoV-2 RT-PCR, ranging from around 50 to 80%. Of note, an in-house swab system was superior to most commercially available sets as reflected by significantly lower Ct values of viral genes. Thus, a simple combination of broadly available materials may enable diagnostic laboratories to bypass global limitations in the supply of swab sets.

Reference

<https://www.nature.com/articles/s41598-021-81782-8>

A new SYBR Green real-time PCR to detect SARS-CoV-2

Abstract

Phylogenetic analysis has demonstrated that the etiologic agent of the 2020 pandemic outbreak is a betacoronavirus named SARS-CoV-2. For public health interventions, a diagnostic test with high sensitivity and specificity is required. The gold standard protocol for diagnosis by the World Health Organization (WHO) is RT-PCR. To detect low viral loads and perform large-scale screening, a low-cost diagnostic test is necessary. Here, a cost-effective test was developed, capable of detecting SARS-CoV-2. An auxiliary protocol was validated for molecular diagnosis with the SYBR Green RT-PCR methodology to successfully screen negative cases of SARS-CoV-2. The results revealed a set of primers with high specificity and no homology with other viruses from the Coronoviridae family or human respiratory tract pathogenic viruses, presenting with complementarity only for rhinoviruses/enteroviruses and Legionella spp. Optimization of the annealing temperature and polymerization time led to a high specificity in the PCR products. A more affordable and swift methodology was developed for negative SARS-CoV-2 screening. This methodology can be applied on a large scale to soften panic and economic burden through guidance for isolation strategies.

Reference

<https://www.nature.com/articles/s41598-021-81245-0>

CD8+ T cells predicted the conversion of common covid-19 to severe

Abstract

To evaluate the predictive effect of T-lymphoid subsets on the conversion of common covid-19 to severe. The laboratory data were collected retrospectively from common covid-19 patients in the First People's Hospital of Zaoyang, Hubei Province, China and the Third People's Hospital of Kunming, Yunnan Province, China, between January 20, 2020 and March 15, 2020 and divided into training set and validation set. Univariate and multivariate logistic regression was performed to investigate the risk factors for the conversion of common covid-19 to severe in the training set, the prediction model was established and verified externally in the validation set. 60 (14.71%) of 408 patients with common covid-19 became severe in 6–10 days after diagnosis. Univariate and multiple

logistic regression analysis revealed that lactate ($P = 0.042$, $OR = 1097.983$, 95% CI 1.303, 924,798.262) and CD8+ T cells ($P = 0.010$, $OR = 0.903$, 95% CI 0.835, 0.975) were independent risk factors for general type patients to turn to severe type. The area under ROC curve of lactate and CD8+ T cells was 0.754 (0.581, 0.928) and 0.842 (0.713, 0.970), respectively. The actual observation value was highly consistent with the prediction model value in curve fitting. The established prediction model was verified in 78 COVID-19 patients in the verification set, the area under the ROC curve was 0.906 (0.861, 0.981), and the calibration curve was consistent. CD8+ T cells, as an independent risk factor, could predict the transition from common covid-19 to severe.

Reference

<https://www.nature.com/articles/s41598-021-81732-4>

Exploring salivary diagnostics in COVID-19: A scoping review and research suggestions

Abstract

Introduction: Molecular diagnostics for SARS-CoV-2 infection characteristically involves the sampling of the throat or nasopharyngeal swab (NPS). However, these procedures are invasive, require necessary skills for sample collection, cause patient discomfort, and are non-conducive for extensive scale testing. Saliva is increasingly being suggested as an alternate diagnostic sample in SARS-CoV-2 infection.

Objectives: This scoping review was done with the objective of exploring the evidence on the role of saliva as an alternate diagnostic sample in SARS-CoV-2 condition.

Methods: Thorough search of the literature in major databases was undertaken in June 2020 using free text and MESH terms, followed by PRISMA to identify 17 studies for data extraction.

Results and conclusions: Evidence was summarised for study characteristics, salivary sampling characteristics, viral load, and longevity of virus in saliva. The literature supports that saliva offers a simple sample collection method compared to technique-sensitive NPS and has the advantage of point-of-care testing for initial screening in community or hospital-based set-up. The additional highlights of this review are

heterogeneity in the current literature and the gaps in methodology. Therefore, a robust study design to generate higher levels of evidence has been proposed.

Reference

<https://www.nature.com/articles/s41405-021-00064-7>

Comprehensive analysis of T cell immunodominance and immunoprevalence of SARS-CoV-2 epitopes in COVID-19 cases

Abstract

T cells are involved in control of SARS-CoV-2 infection. To establish the patterns of immunodominance of different SARS-CoV-2 antigens, and precisely measure virus-specific CD4+ and CD8+ T cells, epitope-specific T cell responses of 99 convalescent COVID-19 cases were studied. The SARS-CoV-2 proteome is probed using 1,925 peptides spanning the entire genome, ensuring an unbiased coverage of HLA alleles for class II responses. For HLA class I, an additional 5,600 predicted binding epitopes for 28 prominent HLA class I alleles was studied, accounting for wide global coverage. We identify several hundred HLA-restricted SARS-CoV-2-derived epitopes. Distinct patterns of immunodominance are observed, which differ for CD4+ T cells, CD8+ T cells, and antibodies. The class I and class II epitopes are combined into epitope megapools to facilitate identification and quantification of SARS-CoV-2-specific CD4+ and CD8+ T cells.

Reference

[https://www.cell.com/cell-reports-medicine/fulltext/S2666-3791\(21\)00015-X](https://www.cell.com/cell-reports-medicine/fulltext/S2666-3791(21)00015-X)

Deletion of the NKG2C receptor encoding KLRC2 gene and HLA-E variants are risk factors for severe COVID-19

Abstract

Purpose: Host genetic variants may contribute to severity of COVID-19. NKG2C+ NK cells are potent antiviral effector cells, potentially limiting the extent of SARS-CoV-2 infections. NKG2C is an activating NK cell receptor encoded by the KLRC2 gene, which binds to HLA-E on infected cells leading to NK cell activation. Heterozygous or homozygous KLRC2 deletion (KLRC2del) may naturally occur and is associated with a

significantly lower or absent NKG2C expression level. In addition, HLA-E*0101/0103 genetic variants occur, caused by a single-nucleotide polymorphism. We therefore investigated whether the severity of COVID-19 is associated with these genetic variants.

Methods: The distribution of KLRC2 deletion and HLA-E*0101/0103 allelic variants in a study cohort of 361 patients were investigated with either mild (N = 92) or severe (N = 269) COVID-19.

Results: Especially the KLRC2del, and at a lower degree the HLA-E*0101, allele were significantly overrepresented in hospitalized patients ($p = 0.0006$ and $p = 0.01$), particularly in patients requiring intensive care ($p < 0.0001$ and $p = 0.01$), compared with patients with mild symptoms. Both genetic variants were independent risk factors for severe COVID-19.

Conclusion: The data show that these genetic variants in the NKG2C/HLA-E axis have a significant impact on the development of severe SARS-CoV-2 infections, and may help to identify patients at high-risk for severe COVID-19.

Reference

<https://www.nature.com/articles/s41436-020-01077-7>

Clinical course of COVID-19 patients needing supplemental oxygen outside the intensive care unit

Abstract

Patients suffering from COVID-19 mostly experience a benign course of the disease. Approximately 14% of SARS-CoV2 infected patients are admitted to a hospital. Cohorts exhibiting severe lung failure in the form of acute respiratory distress syndrome (ARDS) have been well characterized. Patients without ARDS but in need of supplementary oxygen have received much less attention. This study describes the diagnosis, symptoms, treatment and outcomes of hospitalized patients with COVID-19 needing oxygen support during their stay on regular ward. All 133 patients admitted to the RWTH Aachen university hospital with the diagnosis of COVID-19 were included in an observational registry. Clinical data sets were extracted from the hospital information system. This analysis includes all 57 patients requiring supplemental oxygen not admitted to the ICU. 57 patients needing supplemental oxygen and being treated

outside the ICU were analyzed. Patients exhibited the typical set of symptoms for COVID-19. Of note, hypoxic patients mostly did not suffer from clinically relevant dyspnea despite oxygen saturations below 92%. Patients had fever for 7 days and needed supplemental oxygen for 8 days resulting in an overall hospitalization time of 12 days. In addition, patients had persisting systemic inflammation with CRP levels remaining elevated until discharge or death. This description of COVID-19 patients requiring oxygen therapy should be taken into account when planning treatment capacity. Patients on oxygen need long-term inpatient care.

Reference

<https://www.nature.com/articles/s41598-021-81444-9>

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Two-component spike nanoparticle vaccine protects macaques from SARS-CoV-2 infection

Abstract

The SARS-CoV-2 pandemic is continuing to disrupt personal lives, global healthcare systems and economies. Hence, there is an urgent need for a vaccine that prevents viral infection, transmission and disease. Here, we present a two-component protein-based nanoparticle vaccine that displays multiple copies of the SARS-CoV-2 spike protein. Immunization studies show that this vaccine induces potent neutralizing antibody responses in mice, rabbits and cynomolgus macaques. The vaccine-induced immunity protected macaques against a high dose challenge, resulting in strongly reduced viral infection and replication in upper and lower airways. These nanoparticles are a promising vaccine candidate to curtail the SARS-CoV-2 pandemic.

Reference

[https://www.cell.com/cell/fulltext/S0092-8674\(21\)00078-7](https://www.cell.com/cell/fulltext/S0092-8674(21)00078-7)

SARS-CoV-2 vaccination for patients with inflammatory bowel disease: A British Society of Gastroenterology Inflammatory Bowel Disease section and IBD Clinical Research Group position statement

Abstract

SARS-CoV-2 has caused a global health crisis and mass vaccination programmes provide the best opportunity for controlling transmission and protecting populations. Despite the impressive clinical trial results of the BNT162b2 (Pfizer/BioNTech), ChAdOx1 nCoV-19 (Oxford/AstraZeneca), and mRNA-1273 (Moderna) vaccines, important unanswered questions remain, especially in patients with pre-existing conditions. In this position statement endorsed by the British Society of Gastroenterology Inflammatory Bowel Disease (IBD) section and IBD Clinical Research Group, we consider SARS-CoV-2 vaccination strategy in patients with IBD. The risks of SARS-CoV-2 vaccination are anticipated to be very low, and we strongly support SARS-CoV-2 vaccination in patients with IBD. Based on data from previous studies with other vaccines, there are conceptual concerns that protective immune responses to SARS-CoV-2 vaccination may be diminished in some patients with IBD, such as those taking anti-TNF drugs. However, the benefits of vaccination, even in patients treated with anti-TNF drugs, are likely to outweigh these theoretical concerns. Key areas for further research are discussed, including vaccine hesitancy and its effect in the IBD community, the effect of immunosuppression on vaccine efficacy, and the search for predictive biomarkers of vaccine success.

Reference

[https://www.thelancet.com/journals/langas/article/PIIS2468-1253\(21\)00024-8/fulltext](https://www.thelancet.com/journals/langas/article/PIIS2468-1253(21)00024-8/fulltext)

Loss of furin cleavage site attenuates SARS-CoV-2 pathogenesis

Abstract

SARS-CoV-2, a novel coronavirus (CoV)-producing worldwide pandemic, has a furin cleavage site (PRRAR) in its spike protein that is absent in other group 2B CoVs2. To explore whether the furin cleavage site contributes to infection and pathogenesis, we generated a mutant SARS-CoV-2 deleting the furin cleavage site (Δ PRRA). SARS-CoV-2 Δ PRRA replicates had faster kinetics, improved fitness in Vero E6 cells, and reduced

spike protein processing as compared to parental SARS-CoV-2. However, the Δ PRRA mutant had reduced replication in a human respiratory cell line and was attenuated in both hamster and K18-hACE2 transgenic mouse models of SARS-CoV-2 pathogenesis. Despite reduced disease, the Δ PRRA mutant conferred protection against rechallenge with the parental SARS-CoV-2. Importantly, COVID-19 patient sera and receptor-binding domain (RBD) monoclonal antibodies had lower neutralization values against the Δ PRRA mutant versus parental SARS-CoV-2, likely due to increased particle/PFU ratio. Together, these results demonstrate a critical role for the furin cleavage site in SARS-CoV-2 infection and highlight the importance of this site in evaluating antibody neutralization activity.

Reference

<https://www.nature.com/articles/s41586-021-03237-4>

Protective efficacy of a SARS-CoV-2 DNA vaccine in wild-type and immunosuppressed Syrian hamsters

Abstract

A worldwide effort to counter the COVID-19 pandemic has resulted in hundreds of candidate vaccines moving through various stages of research and development, including several vaccines in phase 1, 2 and 3 clinical trials. A relatively small number of these vaccines have been evaluated in SARS-CoV-2 disease models, and fewer in a severe disease model. Here, a SARS-CoV-2 DNA targeting the spike protein and delivered by jet injection, nCoV-S(JET), elicited neutralizing antibodies in hamsters and was protective in both wild-type and transiently immunosuppressed hamster models. This study highlights the DNA vaccine, nCoV-S(JET), which was developed as a great potential to move to next stage of preclinical studies, and it also demonstrates that the transiently-immunosuppressed Syrian hamsters, which recapitulate severe and prolonged COVID-19 disease, can be used for preclinical evaluation of the protective efficacy of spike-based COVID-19 vaccines.

The COVID-19 pandemic has necessitated the rapid development of candidate vaccines and treatments targeting the SARS-CoV-2. Infection with SARS-CoV-2 results in either asymptomatic infection or disease ranging from mild to severe respiratory symptoms. Many factors contribute to the spread of this virus, including a large number

of asymptomatic cases and transmission prior to the onset of symptoms. An effective vaccine would be an invaluable medical countermeasure to protect individuals, prevent transmission, and contribute to containing and ultimately ending this pandemic.

According to the World Health Organization, as of 30 September 2020, there were 41 SARS-CoV-2 vaccines in clinical trials (Phases I, II and III) and 151 vaccines in preclinical development. Of these vaccines in preclinical development several have been tested for immunogenicity in mice and nonhuman primates. Few have been tested in disease models such as the Syrian hamster model. The Syrian hamster has become a leading animal model for SARS-CoV-2 medical countermeasure testing because it does not require a modified virus, or animal, and there are several similarities to human COVID-19 disease including rapid breathing, lethargy, ruffled fur and moderate (<10%) weight loss. Histopathology includes areas of lung consolidation, followed by pneumocyte hyperplasia as the virus is cleared. At least three candidate vaccines have been tested for efficacy in the Syrian hamster model. A Syrian hamster model was developed of severe COVID-19 disease by using cyclophosphamide (CyP) to transiently immunosuppress the hamsters. In this model, lymphopenia is induced by CyP treatment starting 3 days before exposure to virus. After a relatively low dose of virus (1,000 PFU), the immunosuppressed hamsters develop a protracted disease with >15% weight loss over several days and other indicators of severe disease including high levels of virus in the lungs. Herein, it was described the testing of a jet-injected SARS-CoV-2 DNA vaccine in both wild-type and transiently-immunosuppressed hamsters. Hantavirus DNA vaccines administered at a dosage of 0.2 mg are highly immunogenic in hamsters when administered using jet injection. Therefore, as an initial proof-of-concept, we opted to use the 0.2 mg dose.

Reference

<https://www.nature.com/articles/s41541-020-00279-z>

A higher BMI is not associated with a different immune response and disease course in critically ill COVID-19 patients

Abstract

Background/objectives: Obesity appears to be an independent risk factor for ICU admission and a severe disease course in COVID-19 patients. An aberrant

inflammatory response and impaired respiratory function have been suggested as underlying mechanisms. We investigated whether obesity is associated with differences in inflammatory, respiratory, and clinical outcome parameters in critically ill COVID-19 patients.

Subjects/methods: Sixty-seven COVID-19 ICU patients were divided into obese (BMI ≥ 30 kg/m², n = 18, 72% class I obesity, 28% class II obesity) and non-obese (BMI < 30 kg/m², n = 49) groups. Concentrations of circulating interleukin (IL)-6, IL-8, IL-10, tumor necrosis factor alpha (TNF- α), interferon gamma (IFN- γ), interferon gamma-induced protein (IP)-10, monocyte chemoattractant protein (MCP)-1, and IL-1 receptor antagonist (RA) were determined from ICU admission until 10 days afterward, and routine laboratory and clinical parameters were collected.

Results: BMI was 32.6 [31.2–34.5] and 26.0 [24.4–27.7] kg/m² in the obese and non-obese group, respectively. Apart from temperature, which was significantly lower in obese patients (38.1 [36.9–38.9] vs. 38.7 [38.0–39.5] °C, p = 0.02), there were no between-group differences on ICU admission. Plasma cytokine concentrations declined over time (p < 0.05 for all), but no differences between obese and non-obese patients were observed. Also, BMI did not correlate with the cytokine response (IL-6 r = 0.09, p = 0.61, TNF- α r = 0.03, p = 0.99, IP-10 r = 0.28, p = 0.11). The kinetics of clinical inflammatory parameters and respiratory mechanics were also similar in both groups. Finally, no differences in time on ventilator, ICU length of stay or 40-day mortality between obese and non-obese patients were apparent.

Conclusions: In COVID-19 patients requiring mechanical ventilation in the ICU, a higher BMI is not related to a different immunological response, unfavorable respiratory mechanics, or impaired outcome.

Reference

<https://www.nature.com/articles/s41366-021-00747-z>

Global absence and targeting of protective immune states in severe COVID-19

Abstract

While SARS-CoV-2 infection has pleiotropic and systemic effects in some patients, many others experience milder symptoms. We sought a holistic understanding of the

severe/mild distinction in COVID-19 pathology, and its origins. A whole-blood preserving single-cell analysis protocol was performed to integrate contributions from all major cell types including neutrophils, monocytes, platelets, lymphocytes and the contents of serum. Patients with mild COVID-19 disease display a coordinated pattern of interferon-stimulated gene (ISG) expression across every cell population and these cells are systemically absent in patients with severe disease. Severe COVID-19 patients also paradoxically produce very high anti-SARS-CoV-2 antibody titers and have lower viral load as compared to mild disease. Examination of the serum from severe patients demonstrates that they uniquely produce antibodies that functionally block the production of the mild disease-associated ISG-expressing cells, by engaging conserved signaling circuits that dampen cellular responses to interferons. Overzealous antibody responses pit the immune system against itself in many COVID-19 patients and perhaps in other viral infections and this study defines targets for immunotherapies in severe patients to re-engage viral defense.

Reference

<https://www.nature.com/articles/s41586-021-03234-7>

Cross-reactivity of SARS-CoV structural protein antibodies against SARS-CoV-2

Abstract

In the ongoing COVID-19 pandemic, there remain unanswered questions regarding the nature and significance of the humoral immune response towards other coronavirus infections. Here, the cross-reactivity of antibodies was investigated, which was raised against the first SARS-CoV for their reactivity towards SARS-CoV-2. It was extensively characterized that a selection of 10 antibodies covering all of the SARS-CoV structural proteins: spike, membrane, nucleocapsid, and envelope. While nearly all of the examined SARS-CoV antibodies displayed some level of reactivity to SARS-CoV-2, we found only partial cross-neutralization for the spike antibodies. The implications of our work are two-fold. Firstly, a set of antibodies was established with known reactivity to both SARS-CoV and SARS-CoV-2, which will allow further study of both viruses. Secondly, we provide empirical evidence of the high propensity for antibody cross-reactivity between distinct strains of human coronaviruses, critical information for designing diagnostic and vaccine strategies for COVID-19.

Reference

[https://www.cell.com/cell-reports/fulltext/S2211-1247\(21\)00050-4](https://www.cell.com/cell-reports/fulltext/S2211-1247(21)00050-4)

Broad and potent activity against SARS-like viruses by an engineered human monoclonal antibody

Abstract

The recurrent zoonotic spillover of coronaviruses (CoVs) into the human population underscores the need for broadly active countermeasures. We employed a directed evolution approach to engineer three SARS-CoV-2 antibodies for enhanced neutralization breadth and potency. One of the affinity-matured variants, ADG-2, displays strong binding activity to a large panel of sarbecovirus receptor binding domains (RBDs) and neutralizes representative epidemic sarbecoviruses with high potency. Structural and biochemical studies demonstrate that ADG-2 employs a distinct angle of approach to recognize a highly conserved epitope overlapping the receptor binding site. In immunocompetent mouse models of SARS and COVID-19, prophylactic administration of ADG-2 provided complete protection against respiratory burden, viral replication in the lungs, and lung pathology. Altogether, ADG-2 represents a promising broad-spectrum therapeutic candidate against clade 1 sarbecoviruses.

Reference

<https://science.sciencemag.org/content/early/2021/01/22/science.abf4830>

Plitidepsin has potent preclinical efficacy against SARS-CoV-2 by targeting the host protein eEF1A

Abstract

SARS-CoV-2 viral proteins interact with the eukaryotic translation machinery and inhibitors of translation have potent antiviral effects. Here the drug plitidepsin (aplidin) was reported, which has limited clinical approval, possesses antiviral activity (IC₉₀ = 0.88 nM) 27.5-fold more potent than remdesivir against SARS-CoV-2 in vitro, with limited toxicity in cell culture. Through the use of a drug resistant mutant, we show that the antiviral activity of plitidepsin against SARS-CoV-2 is mediated through inhibition of the known target eEF1A. It was demonstrated that the in vivo efficacy of plitidepsin treatment in two mouse models of SARS-CoV-2 infection with a reduction of viral

replication in the lungs by two orders of magnitude using prophylactic treatment. The results indicate that plitidepsin is a promising therapeutic candidate for COVID-19.

Reference

<https://science.sciencemag.org/content/early/2021/01/22/science.abf4058>

Publication Date: Jan 22, 2021

First principle simulation of coated hydroxychloroquine on Ag, Au and Pt nanoparticles

Abstract

From the first month of the COVID-19 pandemic, the potential antiviral properties of hydroxychloroquine (HCQ) and chloroquine (CQ) against SARS-CoV-2 suggested that these drugs could be the appropriate therapeutic candidates. However, their side effects directed clinical tests towards optimizing safe utilization strategies. The noble metal nanoparticles (NP) are promising materials with antiviral and antibacterial properties that can deliver the drug to the target agent, thereby reducing the side effects. In this work, we applied both the quantum mechanical and classical atomistic molecular dynamics approaches to demonstrate the adsorption properties of HCQ/CQ on Ag, Au, AgAu, and Pt nanoparticles. It was found that the adsorption energies of HCQ/CQ towards nanoparticles have the following trend: PtNP > AuNP > AuAgNP > AgNP. This shows that PtNP has the highest affinity in comparison to the other types of nanoparticles. The (non)perturbative effects of this drug on the plasmonic absorption spectra of AgNP and AuNP with the time-dependent density functional theory. The effect of size and composition of NPs on the coating with HCQ and CQ were obtained to propose the appropriate candidate for drug delivery. This kind of modeling could help experimental groups to find efficient and safe therapies.

Reference

<https://www.nature.com/articles/s41598-021-81617-6>

Effect of anakinra versus usual care in adults in hospital with COVID-19 and mild-to-moderate pneumonia (CORIMUNO-ANA-1): A randomised controlled trial

Abstract

Background: Patients with COVID-19 pneumonia have an excess of inflammation and increased concentrations of cytokines including interleukin-1 (IL-1). It was aimed to determine whether anakinra, a recombinant human IL-1 receptor antagonist, could improve outcomes in patients in hospital with mild-to-moderate COVID-19 pneumonia.

Method: In this multicentre, open-label, Bayesian randomised clinical trial (CORIMUNO-ANA-1), nested within the CORIMUNO-19 cohort, we recruited patients from 16 University hospitals in France with mild-to-moderate COVID-19 pneumonia, severe acute respiratory syndrome coronavirus 2 infection confirmed by real-time RT-PCR, requiring at least 3 L/min of oxygen by mask or nasal cannula but without ventilation assistance, a score of 5 on the WHO Clinical Progression Scale (WHO-CPS), and a C-reactive protein serum concentration of more than 25 mg/L not requiring admission to the intensive care unit at admission to hospital. Eligible patients were randomly assigned (1:1) using a web-based secure centralised system, stratified by centre and blocked with varying block sizes (randomly of size two or four), to either usual care plus anakinra (200 mg twice a day on days 1–3, 100 mg twice on day 4, 100 mg once on day 5) or usual care alone. Usual care was provided at the discretion of the site clinicians. The two coprimary outcomes were the proportion of patients who had died or needed non-invasive or mechanical ventilation by day 4 (ie, a score of >5 on the WHO-CPS) and survival without need for mechanical or non-invasive ventilation (including high-flow oxygen) at day 14. All analyses were done on an intention-to-treat basis. The trial is registered with ClinicalTrials.gov, NCT04341584, and is now closed to accrual.

Findings: Between April 8 and April 26, 2020, we screened 153 patients. The study was stopped early following the recommendation of the data and safety monitoring board, after the recruitment of 116 patients: 59 were assigned to the anakinra group, and 57 were assigned to the usual care group. Two patients in the usual care group withdrew consent and were not analysed. In the analysable population, the median age was 66 years (IQR 59 to 76) and 80 (70%) participants were men. In the anakinra group, 21

(36%) of 59 patients had a WHO-CPS score of more than 5 at day 4 versus 21 (38%) of 55 in the usual care group (median posterior absolute risk difference [ARD] -2.5% , 90% credible interval [CrI] -17.1 to 12.0), with a posterior probability of ARD of less than 0 (ie, anakinra better than usual care) of 61.2% . At day 14, 28 (47%; 95% CI 33 to 59) patients in the anakinra group and 28 (51%; 95% CI 36 to 62) in the usual care group needed ventilation or died, with a posterior probability of any efficacy of anakinra (hazard ratio [HR] being less than 1) of 54.5% (median posterior HR 0.97 ; 90% CrI 0.62 to 1.52). At day 90, 16 (27%) patients in the anakinra group and 15 (27%) in the usual care group had died. Serious adverse events occurred in 27 (46%) patients in the anakinra group and 21 (38%) in the usual care group ($p=0.45$).

Interpretation: Anakinra did not improve outcomes in patients with mild-to-moderate COVID-19 pneumonia. Further studies are needed to assess the efficacy of anakinra in other selected groups of patients with more severe COVID-19.

Reference

[https://www.thelancet.com/journals/lanres/article/PIIS2213-2600\(20\)30556-7/fulltext](https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30556-7/fulltext)

SARS-CoV-2 induces robust germinal center CD4 T follicular helper cell responses in rhesus macaques

Abstract

CD4 T follicular helper (Tfh) cells are important for the generation of durable and specific humoral protection against viral infections. The degree to which SARS-CoV-2 infection generates Tfh cells and stimulates the germinal center (GC) response is an important question as we investigate vaccine induced immunity against COVID-19. Here, we report that SARS-CoV-2 infection in rhesus macaques, either infused with convalescent plasma, normal plasma, or receiving no infusion, resulted in transient accumulation of pro-inflammatory monocytes and proliferating Tfh cells with a Th1 profile in peripheral blood. CD4 helper cell responses skewed predominantly toward a Th1 response in blood, lung, and lymph nodes. SARS-CoV-2 Infection induced GC Tfh cells specific for the SARS-CoV-2 spike and nucleocapsid proteins, and a corresponding early appearance of antiviral serum IgG antibodies. Collectively, the data show induction of GC responses in a rhesus model of mild COVID-19.

Reference

<https://www.nature.com/articles/s41467-020-20642-x>

A COVID-19 vaccine candidate using SpyCatcher multimerization of the SARS-CoV-2 spike protein receptor-binding domain induces potent neutralising antibody responses

Abstract

There is need for effective and affordable vaccines against SARS-CoV-2 to tackle the ongoing pandemic. In this study, we describe a protein nanoparticle vaccine against SARS-CoV-2. The vaccine is based on the display of coronavirus spike glycoprotein receptor-binding domain (RBD) on a synthetic virus-like particle (VLP) platform, SpyCatcher003-mi3, using SpyTag/SpyCatcher technology. Low doses of RBD-SpyVLP in a prime-boost regimen induce a strong neutralising antibody response in mice and pigs that is superior to convalescent human sera. Antibody quality was evaluated using ACE2 blocking and neutralisation of cell infection by pseudovirus or wild-type SARS-CoV-2. Using competition assays with a monoclonal antibody panel, it was shown that RBD-SpyVLP induces a polyclonal antibody response that recognises key epitopes on the RBD, reducing the likelihood of selecting neutralisation-escape mutants. Moreover, RBD-SpyVLP is thermostable and can be lyophilised without losing immunogenicity, to facilitate global distribution and reduce cold-chain dependence. The data suggests that RBD-SpyVLP provides strong potential to address clinical and logistic challenges of the COVID-19 pandemic.

Reference

<https://www.nature.com/articles/s41467-020-20654-7>

The impact of quarantine on mental health status among general population in China during the COVID-19 pandemic

Abstract

Quarantine and isolation measures urgently adopted to control the COVID-19 pandemic might potentially have negative psychological and social effects. This cross-sectional, nationwide study was conducted to ascertain the psychological effect of quarantine and identify factors associated with mental health outcomes among population quarantined

to further inform interventions of mitigating mental health risk especially for vulnerable groups under pandemic conditions. Sociodemographic data, attitudes toward the COVID-19, and mental health measurements of 56,679 participants from 34 provinces in China were collected by an online survey from February 28 to March 11, 2020. Of the 56,679 participants included in the study (mean [SD] age, 36.0 [8.2] years), 27,149 (47.9%) were male and 16,454 (29.0%) ever experienced home confinement or centralized quarantine during COVID-19 outbreak. Compared those without quarantine and adjusted for potential confounders, quarantine measures were associated with increased risk of total psychological outcomes (prevalence, 34.1% vs 27.3%; odds ratio [OR], 1.34; 95% CI, 1.28-1.39; $P < 0.001$). Multivariable logistic regression analyses showed that vulnerable groups of the quarantined population included those with pre-existing mental disorders or chronic physical diseases, frontline workers, those in the most severely affected areas during outbreak, infected or suspected patients, and those who are less financially well-off. Complying with quarantine, being able to take part in usual work, and having adequate understanding of information related to the outbreak were associated with less mental health issues. These results suggest that quarantine measures during COVID-19 pandemic are associated with increased risk of experiencing mental health burden, especially for vulnerable groups. Further study is needed to establish interventions to reduce mental health consequences of quarantine and empower wellbeing especially in vulnerable groups under pandemic conditions.

Reference

<https://www.nature.com/articles/s41380-021-01019-y>

Systematic evaluation of IgG responses to SARS-CoV-2 spike protein-derived peptides for monitoring COVID-19 patients

Abstract

Serological tests play an essential role in monitoring and combating the COVID-19 pandemic. Recombinant spike protein (S protein), especially the S1 protein, is one of the major reagents used for serological tests. However, the high cost of S protein production and possible cross-reactivity with other human coronaviruses pose unavoidable challenges. By taking advantage of a peptide microarray with full spike protein coverage, we analyzed 2,434 sera from 858 COVID-19 patients, 63

asymptomatic patients and 610 controls collected from multiple clinical centers. Based on the results, we identified several S protein-derived 12-mer peptides that have high diagnostic performance. In particular, for monitoring the IgG response, one peptide (aa 1148–1159 or S2–78) exhibited a sensitivity (95.5%, 95% CI 93.7–96.9%) and specificity (96.7%, 95% CI 94.8–98.0%) comparable to those of the S1 protein for the detection of both symptomatic and asymptomatic COVID-19 cases. Furthermore, the diagnostic performance of the S2–78 (aa 1148–1159) IgG was successfully validated by ELISA in an independent sample cohort. A panel of four peptides, S1–93 (aa 553–564), S1–97 (aa 577–588), S1–101 (aa 601–612) and S1–105 (aa 625–636), that likely will avoid potential cross-reactivity with sera from patients infected by other coronaviruses was constructed. The peptides identified in this study may be applied independently or in combination with the S1 protein for accurate, affordable, and accessible COVID-19 diagnosis.

Reference

<https://www.nature.com/articles/s41423-020-00612-5>

Publication Date: Jan 21, 2021

Safety and immunogenicity of an inactivated SARS-CoV-2 vaccine, BBV152: A double-blind, randomised, phase 1 trial

Abstract

Background: To mitigate the effects of COVID-19, a vaccine is urgently needed. BBV152 is a whole-virion inactivated SARS-CoV-2 vaccine formulated with a toll-like receptor 7/8 agonist molecule adsorbed to alum (Algel-IMDG) or alum (Algel).

Methods: A double-blind, multicentre, randomised, controlled phase 1 trial was done to assess the safety and immunogenicity of BBV152 at 11 hospitals across India. Healthy adults aged 18–55 years who were deemed healthy by the investigator were eligible. Individuals with positive SARS-CoV-2 nucleic acid and/or serology tests were excluded. Participants were randomly assigned to receive either one of three vaccine formulations (3 µg with Algel-IMDG, 6 µg with Algel-IMDG, or 6 µg with Algel) or an Algel only control vaccine group. Block randomisation was done with a web response platform. Participants and investigators were masked to treatment group allocation. Two

intramuscular doses of vaccines were administered on day 0 (the day of randomisation) and day 14. Primary outcomes were solicited local and systemic reactogenicity events at 2 h and 7 days after vaccination and throughout the full study duration, including serious adverse events. Secondary outcome was seroconversion (at least four-fold increase from baseline) based on wild-type virus neutralisation. Cell-mediated responses were evaluated by intracellular staining and ELISpot. The trial is registered at ClinicalTrials.gov (NCT04471519).

Findings: Between July 13 and 30, 2020, 827 participants were screened, of whom 375 were enrolled. Among the enrolled participants, 100 each were randomly assigned to the three vaccine groups, and 75 were randomly assigned to the control group (Algel only). After both doses, solicited local and systemic adverse reactions were reported by 17 (17%; 95% CI 10·5–26·1) participants in the 3 µg with Algel-IMDG group, 21 (21%; 13·8–30·5) in the 6 µg with Algel-IMDG group, 14 (14%; 8·1–22·7) in the 6 µg with Algel group, and ten (10%; 6·9–23·6) in the Algel-only group. The most common solicited adverse events were injection site pain (17 [5%] of 375 participants), headache (13 [3%]), fatigue (11 [3%]), fever (nine [2%]), and nausea or vomiting (seven [2%]). All solicited adverse events were mild (43 [69%] of 62) or moderate (19 [31%]) and were more frequent after the first dose. One serious adverse event of viral pneumonitis was reported in the 6 µg with Algel group, unrelated to the vaccine. Seroconversion rates (%) were 87·9, 91·9, and 82·8 in the 3 µg with Algel-IMDG, 6 µg with Algel-IMDG, and 6 µg with Algel groups, respectively. CD4+ and CD8+ T-cell responses were detected in a subset of 16 participants from both Algel-IMDG groups.

Interpretation: BBV152 led to tolerable safety outcomes and enhanced immune responses. Both Algel-IMDG formulations were selected for phase 2 immunogenicity trials. Further efficacy trials are warranted.

Reference

[https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(20\)30942-7/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30942-7/fulltext)

COVID-19 vaccines: Where we stand and challenges ahead

Abstract

In the eleven months elapsed since the identification of the SARS-CoV-2 virus and its genome, an exceptional effort by the scientific community has led to the development of over 300 vaccine projects. Over 40 are now undergoing clinical evaluation, ten of these are in Phase III clinical trials, three of them have ended Phase III with positive results. A few of these new vaccines are being approved for emergency use. Existing data suggest that new vaccine candidates may be instrumental in protecting individuals and reducing the spread of pandemic. The conceptual and technological platforms exploited are diverse, and it is likely that different vaccines will show to be better suited to distinct groups of the human population. Moreover, it remains to be elucidated whether and to what extent the capacity of vaccines under evaluation and of unrelated vaccines such as BCG can increase immunological fitness by training innate immunity to SARS-CoV-2 and pathogen-agnostic protection. Due to the short development time and the novelty of the technologies adopted, these vaccines will be deployed with several unresolved issues that only the passage of time will permit to clarify. Technical problems connected with the production of billions of doses and ethical ones connected with the availability of these vaccines also in the poorest countries, are imminent challenges facing us. It is our tenet that in the long run more than one vaccine will be needed to ensure equitable global access, protection of diverse subjects and immunity against viral variants.

Reference

<https://www.nature.com/articles/s41418-020-00720-9>

Network analysis of Down syndrome and SARS-CoV-2 identifies risk and protective factors for COVID-19

Abstract

SARS-CoV-2 infection has spread uncontrollably worldwide while it remains unknown how vulnerable populations, such as Down syndrome (DS) individuals are affected by the COVID-19 pandemic. Individuals with DS have more risk of infections with respiratory complications and present signs of auto-inflammation. They also present with multiple comorbidities that are associated with poorer COVID-19 prognosis in the

general population. All this might place DS individuals at higher risk of SARS-CoV-2 infection or poorer clinical outcomes. In order to get insight into the interplay between DS genes and SARS-cov2 infection and pathogenesis we identified the genes associated with the molecular pathways involved in COVID-19 and the host proteins interacting with viral proteins from SARS-CoV-2. It was then analyzed that overlaps of these genes with HSA21 genes, HSA21 interactors and other genes consistently differentially expressed in DS (using public transcriptomic datasets) and created a DS-SARS-CoV-2 network. It was detected COVID-19 protective and risk factors among HSA21 genes and interactors and/or DS deregulated genes that might affect the susceptibility of individuals with DS both at the infection stage and in the progression to acute respiratory distress syndrome. The analysis suggested that at the infection stage DS individuals might be more susceptible to infection due to triplication of TMPRSS2, that primes the viral S protein for entry in the host cells. However, as the anti-viral interferon I signaling is also upregulated in DS, this might increase the initial anti-viral response, inhibiting viral genome release, viral replication and viral assembly. In the second pro-inflammatory immunopathogenic phase of the infection, the prognosis for DS patients might worsen due to upregulation of inflammatory genes that might favor the typical cytokine storm of COVID-19. It was also detected strong downregulation of the NLRP3 gene, critical for maintenance of homeostasis against pathogenic infections, possibly leading to bacterial infection complications.

Reference

<https://www.nature.com/articles/s41598-021-81451-w>

The effect of SARS-CoV-2 on the prescribing of antimicrobials and analgesics by NHS general dental practitioners in England

Abstract

Aims: To ascertain the effect of SARS-CoV-2 on the utilisation of antibacterial agents and analgesics in primary dental care.

Methods: Antibacterial agents and analgesics (eg paracetamol, aspirin) prescribed in England by general dental practitioners for the periods April-July 2019 and April-July 2020 were analysed.

Results: Antibacterial agents prescribed during COVID-19 restrictions in 2020 (799,282) were higher than a similar time period in 2019 (654,332) by 22%. Amoxicillin was used the most (2020 = 65.0%; 2019 = 66.3%) followed by metronidazole (2020 = 30.2%; 2019 = 28.7%). Erythromycin was prescribed at a similar rate, with lincosamides (clindamycin) prescribed more frequently in 2020 (2020 = 0.6%; 2019 = 0.5%). Clarithromycin was prescribed twice more often in 2020 (0.6%) in comparison to 2019 (0.3%). Co-amoxiclav (0.5%) and phenoxymethylpenicillin (0.3%) were prescribed at a similar rate. Analgesics use increased by 84% (2020 = 28,563; 2019 = 15,507). Use of dihydrocodeine tartrate increased (2020 = 40.9%; 2019 = 32.9%), followed by diclofenac sodium (2020 = 24.6%; 2019 = 12.8%). The opposite trend was seen in relation to ibuprofen with use decreasing (2020 = 19.4%; 2019 = 39.8%) while paracetamol use only slightly increasing (2020 = 15.1%; 2019 = 14.6%).

Conclusions: COVID-19 restrictions on dental care in England resulted in a marked increase in prescribing antibacterial agents and a very marked increase in prescription-only analgesics.

Reference

<https://www.nature.com/articles/s41415-020-2595-2>

Development and comparison of novel multiple cross displacement amplification (MCDA) assays with other nucleic acid amplification methods for SARS-CoV-2 detection

Abstract

The development of alternative isothermal amplification assays including multiple cross displacement amplification (MCDA) may address speed and portability limitations of real-time PCR (rt-PCR) methods for SARS-CoV-2 detection. A novel SARS-CoV-2 MCDA assay was developed and compared its speed and sensitivity to loop-mediated isothermal amplification (LAMP) and rt-PCR. Two MCDA assays targeting SARS-CoV-2 N gene and ORF1ab were designed. The fastest time to detection and sensitivity of MCDA was compared to LAMP and rt-PCR using DNA standards and transcribed RNA. For the N gene, MCDA was faster than LAMP and rt-PCR by 10 and 20 min, respectively with fastest time to detection at 5.2 min. rt-PCR had the highest sensitivity with the limit of detection at 10 copies/ μ l compared with MCDA (100 copies/ μ l) and

LAMP (500 copies/ μ l). For ORF1ab, MCDA and LAMP had similar speed with fastest time to detection at 9.7 and 8.4 min, respectively. LAMP was more sensitive for ORF1ab detection with 50 copies/ μ l compared to MCDA (500 copies/ μ l). In conclusion, different nucleic acid amplification methods provide different advantages. MCDA is the fastest nucleic acid amplification method for SARS-CoV-2 while rt-PCR is the most sensitive. These advantages should be considered when determining the most suitable nucleic acid amplification methods for different applications.

Reference

<https://www.nature.com/articles/s41598-021-81518-8>

[Analysis of SteraMist ionized hydrogen peroxide technology in the sterilization of N95 respirators and other PPE](#)

Abstract

The COVID-19 pandemic has led to widespread shortages of personal protective equipment (PPE) for healthcare workers, including of N95 masks (filtering facepiece respirators; FFRs). These masks are intended for single use but their sterilization and subsequent reuse has the potential to substantially mitigate shortages. Here we investigate PPE sterilization using ionized hydrogen peroxide (iHP), generated by SteraMist equipment (TOMI; Frederick, MD), in a sealed environment chamber. The efficacy of sterilization by iHP was assessed using bacterial spores in biological indicator assemblies. After one or more iHP treatments, five models of N95 masks from three manufacturers were assessed for retention of function based on their ability to form an airtight seal (measured using a quantitative fit test) and filter aerosolized particles. Filtration testing was performed at a university lab and at a National Institute for Occupational Safety and Health (NIOSH) pre-certification laboratory. The data demonstrate that N95 masks sterilized using SteraMist iHP technology retain filtration efficiency up to ten cycles, the maximum number tested to date. A typical iHP environment chamber with a volume of ~ 80 m³ can treat ~ 7000 masks and other items (e.g. other PPE, iPADs), making this an effective approach for a busy medical center.

Reference

<https://www.nature.com/articles/s41598-021-81365-7>

The SARS-CoV-2 nucleocapsid phosphoprotein forms mutually exclusive condensates with RNA and the membrane-associated M protein

Abstract

The multifunctional nucleocapsid (N) protein in SARS-CoV-2 binds the ~30 kb viral RNA genome to aid its packaging into the 80–90 nm membrane-enveloped virion. The N protein is composed of N-terminal RNA-binding and C-terminal dimerization domains that are flanked by three intrinsically disordered regions. Here it was demonstrated that the N protein's central disordered domain drives phase separation with RNA, and that phosphorylation of an adjacent serine/arginine rich region modulates the physical properties of the resulting condensates. In cells, N forms condensates that recruit the stress granule protein G3BP1, highlighting a potential role for N in G3BP1 sequestration and stress granule inhibition. The SARS-CoV-2 membrane (M) protein independently induces N protein phase separation, and three-component mixtures of N + M + RNA form condensates with mutually exclusive compartments containing N + M or N + RNA, including annular structures in which the M protein coats the outside of an N + RNA condensate. These findings support a model in which phase separation of the SARS-CoV-2 N protein contributes both to suppression of the G3BP1-dependent host immune response and to packaging genomic RNA during virion assembly.

Reference

<https://www.nature.com/articles/s41467-020-20768-y>

Tracking and promoting the usage of a COVID-19 contact tracing app

Abstract

Digital contact tracing apps have been introduced globally as an instrument to contain the COVID-19 pandemic. Yet, privacy by design impedes both the evaluation of these tools and the deployment of evidence-based interventions to stimulate uptake. An online panel survey was combined with mobile tracking data to measure the actual usage of Germany's official contact tracing app and reveal higher uptake rates among respondents with an increased risk of severe illness, but lower rates among those with a heightened risk of exposure to COVID-19. Using a randomized intervention, it was shown that informative and motivational video messages have very limited effect on

uptake. However, findings from a second intervention suggest that even small monetary incentives can strongly increase uptake and help make digital contact tracing a more effective tool.

Reference

<https://www.nature.com/articles/s41562-020-01044-x>

High expression of ACE2 and TMPRSS2 and clinical characteristics of COVID-19 in colorectal cancer patients

Abstract

Little is known of the patterns of expression of ACE2 and TMPRSS2 or the clinical characteristics of COVID-19 in patients with COVID-19 and colorectal cancer. It was found in both bulk and single-cell RNA-seq profiles that ACE2 and TMPRSS2 were expressed at high levels on tumor and normal colorectal epithelial tissues. Clinically, patients with colorectal cancer and COVID-19 were more likely to have lymphopenia, higher respiratory rate, and high hypersensitive C-reactive protein levels than matched patients with COVID-19 but without cancer. These results suggest that patients with colorectal cancer may be particularly susceptible to SARS-CoV-2 infection. Further mechanistic studies are needed to support our findings.

Reference

<https://www.nature.com/articles/s41698-020-00139-y>

Self-organized wavy infection curve of COVID-19

Abstract

Exploiting the SIQR model for COVID-19, I show that the wavy infection curve in Japan is the result of fluctuation of policy on isolation measure imposed by the government and obeyed by citizens. Assuming the infection coefficient be a two-valued function of the number of daily confirmed new cases, I show that when the removal rate of infected individuals is between these two values, the wavy infection curve is self-organized. On the basis of the infection curve, I classify the outbreak of COVID-19 into five types and show that these differences can be related to the relative magnitude of the transmission coefficient and the quarantine rate of infected individuals.

Reference

<https://www.nature.com/articles/s41598-021-81521-z>

SARS-CoV-2 neutralizing antibodies in patients with varying severity of acute COVID-19 illness

Abstract

In order to support vaccine development, and to aid convalescent plasma therapy, it would be important to understand the kinetics, timing and persistence of SARS-CoV-2 neutralizing antibodies (NAbs), and their association with clinical disease severity. Therefore, we used a surrogate viral neutralization test to evaluate their levels in patients with varying severity of illness, in those with prolonged shedding and those with mild/asymptomatic illness at various time points. Patients with severe or moderate COVID-19 illness had earlier appearance of NAbs at higher levels compared to those with mild or asymptomatic illness. Furthermore, those who had prolonged shedding of the virus, had NAbs appearing faster and at higher levels than those who cleared the virus earlier. During the first week of illness the NAb levels of those with mild illness was significantly less ($p = 0.01$), compared to those with moderate and severe illness. At the end of 4 weeks (28 days), although 89% had NAbs, 38/76 (50%) in those with > 90 days had a negative result for the presence of NAbs. The Ab levels significantly declined during convalescence (> 90 days since onset of illness), compared to 4 to 8 weeks since onset of illness. Our data show that high levels of NAbs during early illness associated with clinical disease severity and that these antibodies declined in 50% of individuals after 3 months since onset of illness.

Reference

<https://www.nature.com/articles/s41598-021-81629-2>

Autumn COVID-19 surge dates in Europe correlated to latitudes, not to temperature-humidity, pointing to vitamin D as contributing factor

Abstract

To determine the factor triggering the sudden surge of daily new COVID-19 cases arising in most European countries during the autumn of 2020. The dates of the surge were determined using a fitting of the two last months of reported daily new cases in 18

European countries with latitude ranging from 39° to 62°. The study proves no correlation between the country surge date and the 2 weeks preceding temperature or humidity but shows an impressive linear correlation with latitude. The country surge date corresponds to the time when its sun UV daily dose drops below $\approx 34\%$ of that of 0° latitude. Introducing reported seasonal blood 25-hydroxyvitamin D (25(OH)D) concentration variation into the reported link between acute respiratory tract infection risk and 25(OH)D concentration quantitatively explains the surge dynamics. Several studies have already substantiated a 25(OH)D concentration impact on COVID-19 severity. However, by comparing different patient populations, discriminating whether a low 25(OH)D concentration is a real factor underlying COVID-19 severity or only a marker of another weakness that is the primary severity factor can be challenging. The date of the surge is an intrapopulation observation and has the benefit of being triggered only by a parameter globally affecting the population, i.e. decreases in the sun UV daily dose. The results indicate that a low 25(OH)D concentration is a contributing factor to COVID-19 severity, which, combined with previous studies, provides a convincing set of evidence.

Reference

<https://www.nature.com/articles/s41598-021-81419-w>

Global pandemics interconnected — obesity, impaired metabolic health and COVID-19

Abstract

Obesity and impaired metabolic health are established risk factors for the non-communicable diseases (NCDs) type 2 diabetes mellitus, cardiovascular disease, neurodegenerative diseases, cancer and nonalcoholic fatty liver disease, otherwise known as metabolic associated fatty liver disease (MAFLD). With the worldwide spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), obesity and impaired metabolic health also emerged as important determinants of severe coronavirus disease 2019 (COVID-19). Furthermore, novel findings indicate that specifically visceral obesity and characteristics of impaired metabolic health such as hyperglycaemia, hypertension and subclinical inflammation are associated with a high risk of severe COVID-19. In this Review, it was highlighted that how obesity and

impaired metabolic health increase complications and mortality in COVID-19. It was also summarized that the consequences of SARS-CoV-2 infection for organ function and risk of NCDs. In addition, it was discussed that data indicating that the COVID-19 pandemic could have serious consequences for the obesity epidemic. As obesity and impaired metabolic health are both accelerators and consequences of severe COVID-19, and might adversely influence the efficacy of COVID-19 vaccines, strategies were proposed for the prevention and treatment of obesity and impaired metabolic health on a clinical and population level, particularly while the COVID-19 pandemic is present.

Reference

<https://www.nature.com/articles/s41574-020-00462-1>

Discriminating mild from critical COVID-19 by innate and adaptive immune single-cell profiling of bronchoalveolar lavages

Abstract

How the innate and adaptive host immune system miscommunicate to worsen COVID-19 immunopathology has not been fully elucidated. Here, single-cell deep-immune profiling of bronchoalveolar lavage (BAL) samples were performed from 5 patients with mild and 26 with critical COVID-19 in comparison to BALs from non-COVID-19 pneumonia and normal lung. Pseudotime inference was used to build T-cell and monocyte-to-macrophage trajectories and model gene expression changes along them. In mild COVID-19, CD8⁺ resident-memory (TRM) and CD4⁺ T-helper-17 (TH17) cells undergo active (presumably antigen-driven) expansion towards the end of the trajectory, and are characterized by good effector functions, while in critical COVID-19 they remain more naïve. Vice versa, CD4⁺ T-cells with T-helper-1 characteristics (TH1-like) and CD8⁺ T-cells expressing exhaustion markers (TEX-like) are enriched halfway their trajectories in mild COVID-19, where they also exhibit good effector functions, while in critical COVID-19 they show evidence of inflammation-associated stress at the end of their trajectories. Monocyte-to-macrophage trajectories show that chronic hyperinflammatory monocytes are enriched in critical COVID-19, while alveolar macrophages, otherwise characterized by anti-inflammatory and antigen-presenting characteristics, are depleted. In critical COVID-19, monocytes contribute to an ATP-purinergic signaling-inflammasome footprint that could enable COVID-19 associated

fibrosis and worsen disease-severity. Finally, viral RNA-tracking reveals infected lung epithelial cells, and a significant proportion of neutrophils and macrophages that are involved in viral clearance.

Reference

<https://www.nature.com/articles/s41422-020-00455-9>

The presentation of SARS-CoV-2 peptides by the common HLA-A*02:01 molecule

Abstract

CD8⁺ T cells are crucial for anti-viral immunity, however, understanding T cell responses requires the identification of epitopes presented by Human Leukocyte Antigens (HLA). To date, few SARS-CoV-2-specific CD8⁺ T cell epitopes have been described. Internal viral proteins are typically more conserved than surface proteins and are often the target of CD8⁺ T cells. Therefore, we have characterised eight peptides derived from the internal SARS-CoV-2 Nucleocapsid protein predicted to bind HLA-A*02:01, the most common HLA molecule in the global population. It was determined that not all peptides could form a complex with HLA-A*02:01, and the six crystal structures determined revealed that some peptides adopted a mobile conformation. We therefore provide a molecular understanding of SARS-CoV-2 CD8⁺ T cell epitopes. Furthermore, it was shown that there is limited pre-existing CD8⁺ T cell response towards these epitopes in unexposed individuals. Together, these data show that SARS-CoV-2 Nucleocapsid might not contain potent epitopes restricted to HLA-A*02:01.

Reference

[https://www.cell.com/iscience/fulltext/S2589-0042\(21\)00064-X](https://www.cell.com/iscience/fulltext/S2589-0042(21)00064-X)

Early induction of functional SARS-CoV-2-specific T cells associates with rapid viral clearance and mild disease in COVID-19 patients

Abstract

Virus-specific humoral and cellular immunity act synergistically to protect the host from viral infection. The dynamic changes of virological and immunological parameters were interrogated in 12 patients with symptomatic acute SARS-CoV-2 infection from disease

onset to convalescence or death. SARS-CoV-2 viral RNA in the respiratory tract were quantified in parallel with antibodies and circulating T cells specific for various structural (nucleoprotein [NP], membrane [M], ORF3a, and spike) and non-structural (ORF7/8, NSP7, and NSP13) proteins. Although rapid induction and quantity of humoral responses associate with an increase in disease severity, early induction of interferon (IFN)- γ -secreting SARS-CoV-2-specific T cells is present in patients with mild disease and accelerated viral clearance. These findings provide support for the prognostic value of early functional SARS-CoV-2-specific T cells with important implications in vaccine design and immune monitoring.

Reference

[https://www.cell.com/cell-reports/fulltext/S2211-1247\(21\)00041-3](https://www.cell.com/cell-reports/fulltext/S2211-1247(21)00041-3)

Model-informed COVID-19 vaccine prioritization strategies by age and serostatus

Abstract

Limited initial supply of SARS-CoV-2 vaccine raises the question of how to prioritize available doses. Here, a mathematical model was used to compare five age-stratified prioritization strategies. A highly effective transmission-blocking vaccine prioritized to adults ages 20-49 years minimized cumulative incidence, but mortality and years of life lost were minimized in most scenarios when the vaccine was prioritized to adults over 60 years old. Use of individual-level serological tests to redirect doses to seronegative individuals improved the marginal impact of each dose while potentially reducing existing inequities in COVID-19 impact. While maximum impact prioritization strategies were broadly consistent across countries, transmission rates, vaccination rollout speeds, and estimates of naturally acquired immunity, this framework can be used to compare impacts of prioritization strategies across contexts.

Reference

<https://science.sciencemag.org/content/early/2021/01/21/science.abe6959>

Diabetes, obesity, metabolism and SARS-CoV-2 infection: The end of the beginning

Abstract

The increased prevalence of obesity, diabetes and cardiovascular risk factors in people hospitalized with severe COVID-19 illness has engendered considerable interest in the metabolic aspects of SARS-CoV-2-induced pathophysiology. Here, concepts were updated that were informing how metabolic disorders and their comorbidities modify the susceptibility to, natural history and potential treatment of SARS-CoV-2 infection, with a focus on human biology. New data informing genetic predisposition, epidemiology, immune responses, disease severity and therapy of COVID-19 in people with obesity and diabetes are highlighted. The emerging relationships of metabolic disorders to viral-induced immune responses and viral persistence, and the putative importance of adipose and islet ACE2 expression, glycemic control, cholesterol metabolism, and glucose- and lipid-lowering drugs is reviewed, with attention to controversies and unresolved questions. Rapid progress in these areas informs our growing understanding of SARS-CoV-2 infection in people with diabetes and obesity, while refining the therapeutic strategies and research priorities in this vulnerable population.

Reference

[https://www.cell.com/cell-metabolism/fulltext/S1550-4131\(21\)00016-4](https://www.cell.com/cell-metabolism/fulltext/S1550-4131(21)00016-4)

PERSPECTIVE

Publication Date: Jan 21, 2021

Optimizing age-specific vaccination

Efficacious vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have been developed, tested, and approved for emergency use with unprecedented speed. Deployment of multiple vaccines was initiated in several countries less than 1 year after identification of the virus. Although vaccine production is being rapidly scaled up, demand will exceed supply for the next several months. Consequently, an urgent challenge is the optimization of vaccine allocation to maximize public health benefit. Bubar *et al.* demonstrate that vaccination of older people is the optimal age-based strategy to alleviate the burden of COVID-19. Although vaccination of younger adults is projected to avert the greatest incidence, vaccinating older adults will most effectively reduce mortality. In addition, they assess targeted vaccination that was based on serological status, finding that vaccinating seronegative individuals improves efficiency especially in settings where seroprevalence is high. To vanquish a pathogen that causes such steeply divergent case fatality rates as that of SARS-CoV-2, the optimal strategy is clear: Directly vaccinate those with greatest personal risk. For more details, read the link given below.

Reference

<https://science.sciencemag.org/content/early/2021/01/21/science.abg2334>

COMMENT

Publication Date: Jan 27, 2021

United by the global COVID-19 pandemic: Divided by our values and viral identities

The rapidly evolving landscape of the global COVID-19 pandemic necessitates urgent scientific advances and adaptive behavioural and policy responses to contain viral transmission, reduce impacts on public health, and minimise societal disruption. Epidemiological models of SARS-CoV-2 transmission are heavily influencing policy responses, forecasting viral infection, transmission, and death rates under simplified representations of human behaviour. They either assume that all members of a population or demographic group behave identically or design individual behavioural decision rules based on demographic and mobility data. In pluralistic societies, however, individual behavioural responses vary with personal values, situational contexts, and social group identities, affecting policy compliance and viral transmission. Here, it was identified and explored that the impacts of salient viral identities or “COVID-19 personality types” that are emerging and fluidly coalescing with each other and existing social and political identities. The resultant heightened inter-group differentiation explains the politicisation of the pandemic and rampant racism, discrimination, and conflict observed now and with epidemics historically. Recognising salient COVID-19 behavioural identities can improve scientific forecasting of SARS-CoV-2 transmission and the likely impact of containment measures, as well as tailor nuanced policies and communications to enhance individual coping and compliance. As governments contemplate easing social-distancing restrictions, the science-society-policy nexus needs fortification through public participation, structured deliberation, and evidence-informed decision-making of policy options to negotiate the complex value trade-offs among public health, the market economy, and civil liberty. By thus valuing human diversity to foster societal resilience, an ethical agenda can be set with a united response to the COVID-19 pandemic and global commons challenges whose impacts are less immediate, but no less dire for humanity.

Reference

<https://www.nature.com/articles/s41599-020-00679-5>

REPORT

Publication Date: Jan 26, 2021

The immunodominant and neutralization linear epitopes for SARS-CoV-2

Although vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are under development, the antigen epitopes on the virus and their immunogenicity are poorly understood. Here, it was simulated that the 3D structures and predict the B cell epitopes on the spike (S), envelope (E), membrane (M), and nucleocapsid (N) proteins of SARS-CoV-2 using structure-based approaches and validate epitope immunogenicity by immunizing mice. Almost all 33 predicted epitopes effectively induce antibody production, six of these are immunodominant epitopes in individuals, and 23 are conserved within SARS-CoV-2, SARS-CoV, and bat coronavirus RaTG13. It was found that the immunodominant epitopes of individuals with domestic (China) SARS-CoV-2 are different from those of individuals with imported (Europe) SARS-CoV-2, which may be caused by mutations on the S (G614D) and N proteins. Importantly, we find several epitopes on the S protein that elicit neutralizing antibodies against D614 and G614 SARS-CoV-2, which can contribute to vaccine design against coronaviruses.

Reference

[https://www.cell.com/cell-reports/fulltext/S2211-1247\(20\)31655-7](https://www.cell.com/cell-reports/fulltext/S2211-1247(20)31655-7)

Publication Date: Jan 25, 2021

Prospective mapping of viral mutations that escape antibodies used to treat COVID-19

Antibodies are a potential therapy for SARS-CoV-2, but the risk of the virus evolving to escape them remains unclear. Here we map how all mutations to SARS-CoV-2's receptor-binding domain (RBD) affect binding by the antibodies in the REGN-COV2 cocktail and the antibody LY-CoV016. These complete maps uncover a single amino-acid mutation that fully escapes the REGN-COV2 cocktail, which consists of two antibodies targeting distinct structural epitopes. The maps also identify viral mutations

that are selected in a persistently infected patient treated with REGN-COV2, as well as during in vitro viral escape selections. Finally, the maps reveal that mutations escaping the individual antibodies are already present in circulating SARS-CoV-2 strains. Overall, these complete escape maps enable interpretation of the consequences of mutations observed during viral surveillance.

Reference

<https://science.sciencemag.org/content/early/2021/01/22/science.abf9302>