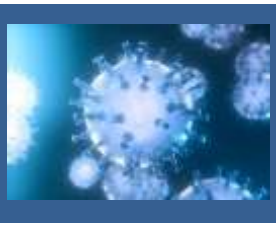
COVID-19

Nov 18 – 24, 2021



RESEARCH PUBLICATIONS

Publication Date: Nov 24, 2021

SARS-CoV-2 virus transfers to skin through contact with contaminated solids

Abstract

Transfer of SARS-CoV-2 from solids to fingers is one step in infection *via* contaminated solids, and the possibility of infection from this route has driven calls for increased frequency of handwashing during the COVID-19 pandemic. To analyze this route of infection, we measured the percentage of SARS-CoV-2 that was transferred from a solid to an artificial finger. A droplet of SARS-CoV-2 suspension (1 µL) was placed on a solid, and then artificial skin was briefly pressed against the solid with a light force (3 N). Transfer from a variety of solids was detected, and transfer from the non-porous solids, glass, stainless steel, and Teflon, was substantial when the droplet was still wet. The viral titer for the finger was 13–16% or 0.8–0.9 log less than for the input droplet. Transfer still occurred after the droplet evaporated, but was smaller, 3–9%. We found a lower level of transfer from porous solids but did not find a significant effect of solid wettability for non-porous solids.

Reference

https://www.nature.com/articles/s41598-021-00843-0

The N501Y spike substitution enhances SARS-CoV-2 infection and transmission

Abstract

Beginning in the summer of 2020, a variant of SARS-CoV-2, the cause of the COVID-19 pandemic, emerged in the United Kingdom. This B.1.1.7 variant, also known as Alpha, increased rapidly in prevalence, attributed to an increase in infection and/or transmission efficiency. The Alpha variant has 19 nonsynonymous mutations across its

viral genome, including 8 substitutions or deletions in the spike protein, which interacts with cellular receptors to mediate infection and tropism. Here, using a reverse genetics approach, we show that, of the 8 individual spike protein substitutions, only N501Y exhibited consistent fitness gains for replication in the upper airway in the hamster model as well as primary human airway epithelial cells. The N501Y substitution recapitulated the phenotype of enhanced viral transmission seen with the combined 8 Alpha spike mutations, suggesting it is a major determinant of increased transmission of this variant. Mechanistically, the N501Y substitution improved the affinity of the viral spike protein for cellular receptors. As suggested by its convergent evolution in Brazil, South Africa, and elsewhere, our results indicate that N501Y substitution is a major adaptive spike mutation of major concern.

Reference

https://www.nature.com/articles/s41586-021-04245-0

Correlates of neutralizing/SARS-CoV-2-S1-binding antibody response with adverse effects and immune kinetics in BNT162b2-vaccinated individuals

Abstract

While mRNA vaccines against SARS-CoV-2 are exceedingly effective in preventing symptomatic infection, their immune response features remain to be clarified. In the present prospective study, 225 healthy individuals in Japan, who received two BNT162b2 doses, were enrolled. Correlates of BNT162b2-elicited SARS-CoV-2-neutralizing activity (50% neutralization titer: NT50; assessed using infectious virions) with various determinants were examined and the potency of sera against variants of concerns was determined. Significant rise in NT50s was seen in sera on day 28 post-1st dose. A moderate inverse correlation was seen between NT50s and ages, but no correlation seen between NT50s and adverse effects. NT50s and SARS-CoV-2-S1-binding-IgG levels on day 28 post-1st dose and pain scores following the 2nd dose were greater in women than in men. The average half-life of NT50s was ~ 68 days, and 23.6% (49 out of 208 individuals) failed to show detectable neutralizing activity on day 150. While sera from elite-responders (NT50s > 1,500: the top 4% among the participants) potently to moderately blocked all variants of concerns examined, some sera with low NT50s failed to block the B.1.351-beta strain. Since BNT162b2-elicited

immunity against SARS-CoV-2 is short, an additional vaccine or other protective measures are needed.

Reference

https://www.nature.com/articles/s41598-021-01930-y

Association of lockdowns with the protective role of ultraviolet-B (UVB) radiation in reducing COVID-19 deaths

Abstract

Nations are imposing unprecedented measures at a large scale to contain the spread of the COVID-19 pandemic. While recent studies show that non-pharmaceutical intervention measures such as lockdowns may have mitigated the spread of COVID-19, those measures also lead to substantial economic and social costs, and might limit exposure to ultraviolet-B radiation (UVB). Emerging observational evidence indicates the protective role of UVB and vitamin D in reducing the severity and mortality of COVID-19 deaths. This observational study empirically outlines the protective roles of lockdown and UVB exposure as measured by the ultraviolet index (UVI). Specifically, we examine whether the severity of lockdown is associated with a reduction in the protective role of UVB exposure. A log-linear fixed-effects model was used on a panel dataset of secondary data of 155 countries from 22 January 2020 until 7 October 2020 ($n = 29{,}327$). The cumulative number of COVID-19 deaths was used as the dependent variable and the mitigating influence of lockdown severity was isolated on the association between UVI and growth rates of COVID-19 deaths from time-constant country-specific and time-varying country-specific potentially confounding factors. After controlling for time-constant and time-varying factors, we find that a unit increase in UVI and lockdown severity are independently associated with -0.85 percentage points (p.p) and -4.7 p.p decline in COVID-19 deaths growth rate, indicating their respective protective roles. The change of UVI over time is typically large (e.g., on average, UVI in New York City increases up to 6 units between January until June), indicating that the protective role of UVI might be substantial. However, the widely utilized and least severe lockdown (governmental recommendation to not leave the house) is associated with the mitigation of the protective role of UVI by 81% (0.76 p.p), which indicates a downside risk associated with its widespread use. It was found that lockdown severity

and UVI are independently associated with a slowdown in the daily growth rates of cumulative COVID-19 deaths. However, evidence was found that an increase in lockdown severity is associated with significant mitigation in the protective role of UVI in reducing COVID-19 deaths. The results suggest that lockdowns in conjunction with adequate exposure to UVB radiation might have even reduced the number of COVID-19 deaths more strongly than lockdowns alone. For example, it was estimated that there would be 11% fewer deaths on average with sufficient UVB exposure during the period people were recommended not to leave their house. Therefore, the study outlines the importance of considering UVB exposure, especially while implementing lockdowns, and could inspire further clinical studies that may support policy decision-making in countries imposing such measures.

Reference

https://www.nature.com/articles/s41598-021-01908-w

In silico **evaluation of the interaction between ACE2 and SARS-CoV-2 Spike protein in a hyperglycemic environment**

Abstract

The worse outcome of COVID-19 in people with diabetes mellitus could be related to the non-enzymatic glycation of human ACE2, leading to a more susceptible interaction with virus Spike protein. It was aimed to evaluate, through a computational approach, the interaction between human ACE2 receptor and SARS-CoV-2 Spike protein under different conditions of hyperglycemic environment. A computational analysis was performed, based on the X-ray crystallographic structure of the Spike Receptor-Binding Domain (RBD)-ACE2 system. The possible scenarios of lysine aminoacid residues on surface transformed by glycation were considered: (1) on ACE2 receptor; (2) on Spike protein; (3) on both ACE2 receptor and Spike protein. In comparison to the native condition, the number of polar bonds (comprising both hydrogen bonds and salt bridges) in the poses considered are 10, 6, 6, and 4 for the states ACE2/Spike both native, ACE2 native/Spike glycated, ACE2 glycated/Spike native, ACE2/Spike both glycated, respectively. The analysis highlighted also how the number of non-polar contacts (in this case, van der Waals and aromatic interactions) significantly decreases when the lysine aminoacid residues undergo glycation. Following non-enzymatic

glycation, the number of interactions between human ACE2 receptor and SARS-CoV-2 Spike protein is decreased in comparison to the unmodified model. The reduced affinity of the Spike protein for ACE2 receptor in case of non-enzymatic glycation may shift the virus to multiple alternative entry routes.

Reference

https://www.nature.com/articles/s41598-021-02297-w

Diagnostic performance of rapid antigen tests (RATs) for SARS-CoV-2 and their efficacy in monitoring the infectiousness of COVID-19 patients

Abstract

The most widely used test for the diagnosis of SARS-CoV-2 infection is a PCR test. PCR has very high sensitivity and is able to detect very low amounts of RNA. However, many individuals receiving a positive test result in a context of a PCR-based surveillance might be infected with SARS-CoV-2, but they are not contagious at the time of the test. The question arise regards if the cost effective, portable rapid antigen tests (RATs) have a better performance than PCR in identification of infectious individuals. In this direction, we examined the diagnostic performance of RATs from 14 different manufacturers in 400 clinical samples with known rRT-PCR cycles threshold (cT) and 50 control samples. Substantial variability was observed in the limit of detection (LOD) of different RATs ($cT = 26.8–34.7$). The fluorescence-based RAT exhibited a LOD of $cT = 34.7$. The use of the most effective RATs leads to true positive rates (sensitivities) of 99.1% and 90.9% for samples with $cT \leq 30$ and $cT \leq 33$, respectively, percentages that can guarantee a sensitivity high enough to identify contagious patients. RAT testing may also substantially reduce the quarantine period for infected individuals without compromising personal or public safety.

Reference

https://www.nature.com/articles/s41598-021-02197-z

Administration of aerosolized SARS-CoV-2 to K18-hACE2 mice uncouples respiratory infection from fatal neuroinvasion

Abstract

The development of a tractable small animal model faithfully reproducing human COVID-19 pathogenesis would arguably meet a pressing need in biomedical research. Thus far, most investigators have used transgenic mice expressing the human ACE2 in epithelial cells (K18-hACE2 transgenic mice) that are intranasally instilled with a liquid SARS-CoV-2 suspension under deep anesthesia. Unfortunately, this experimental approach results in disproportionate high CNS infection leading to fatal encephalitis, which is rarely observed in humans and severely limits this model's usefulness. Here, we describe the use of an inhalation tower system that allows exposure of unanesthetized mice to aerosolized virus under controlled conditions. Aerosol exposure of K18-hACE2 transgenic mice to SARS-CoV-2 resulted in robust viral replication in the respiratory tract, anosmia, and airway obstruction, but did not lead to fatal viral neuroinvasion. When compared to intranasal inoculation, aerosol infection resulted in a more pronounced lung pathology including increased immune infiltration, fibrin deposition and a transcriptional signature comparable to that observed in SARS-CoV-2-infected patients. This model may prove useful for studies of viral transmission, disease pathogenesis (including long-term consequences of SARS-CoV-2 infection) and therapeutic interventions.

Reference

https://www.science.org/doi/10.1126/sciimmunol.abl9929

Immune correlates analysis of the mRNA-1273 COVID-19 vaccine efficacy clinical trial

Abstract

In the coronavirus efficacy (COVE) phase 3 clinical trial, vaccine recipients were assessed for neutralizing and binding antibodies as correlates of risk for COVID-19 disease and as correlates of protection. These immune markers were measured at second vaccination and 4 weeks later, with values reported in standardized WHO

International Units. All markers were inversely associated with COVID-19 risk and directly associated with vaccine efficacy. Vaccine recipients with post-vaccination 50% neutralization titers 10, 100, and 1000 had estimated vaccine efficacy of 78% (95% confidence interval 54, 89%), 91% (87, 94%), and 96% (94, 98%), respectively. These results help define immune marker correlates of protection and may guide approval decisions for mRNA COVID-19 vaccines and other COVID-19 vaccines.

Reference

https://www.science.org/doi/10.1126/science.abm3425

Adaptation, spread and transmission of SARS-CoV-2 in farmed minks and associated humans in the Netherlands

Abstract

In the first wave of the COVID-19 pandemic (April 2020), SARS-CoV-2 was detected in farmed minks and genomic sequencing was performed on mink farms and farm personnel. Here, the outbreak and use sequence data wer described with Bayesian phylodynamic methods to explore SARS-CoV-2 transmission in minks and humans on farms. High number of farm infections (68/126) in minks and farm workers (>50% of farms) were detected, with limited community spread. Three of five initial introductions of SARS-CoV-2 led to subsequent spread between mink farms until November 2020. Viruses belonging to the largest cluster acquired an amino acid substitution in the receptor binding domain of the Spike protein (position 486), evolved faster and spread longer and more widely. Movement of people and distance between farms were statistically significant predictors of virus dispersal between farms. The study provides novel insights into SARS-CoV-2 transmission between mink farms and highlights the importance of combining genetic information with epidemiological information when investigating outbreaks at the animal-human interface.

Reference

https://www.nature.com/articles/s41467-021-27096-9

An integrated method for optimized identification of effective natural inhibitors against SARS-CoV-2 3CLpro

Abstract

The current severe situation of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has not been reversed and posed great threats to global health. Therefore, there is an urgent need to find out effective antiviral drugs. The 3-chymotrypsin-like protease (3CLpro) in SARS-CoV-2 serve as a promising anti-virus target due to its essential role in the regulation of virus reproduction. Here, an improved integrated approach was reported to identify effective 3CLpro inhibitors from effective Chinese herbal formulas. With this approach, we identified the 5 natural products (NPs) including narcissoside, kaempferol-3-O-gentiobioside, rutin, vicenin-2 and isoschaftoside as potential anti-SARS-CoV-2 candidates. Subsequent molecular dynamics simulation additionally revealed that these molecules can be tightly bound to 3CLpro and confirmed effectiveness against COVID-19. Moreover, kaempferol-3-o-gentiobioside, vicenin-2 and isoschaftoside were first reported to have SARS-CoV-2 3CLpro inhibitory activity. In summary, this optimized integrated strategy for drug screening can be utilized in the discovery of antiviral drugs to achieve rapid acquisition of drugs with specific effects on antiviral targets.

Reference

https://www.nature.com/articles/s41598-021-02266-3

SARS-CoV-2 receptor binding domain radio-probe: A non-invasive approach for angiotensin-converting enzyme 2 mapping in mice

Abstract

The spike protein of SARS-CoV-2 interacts with angiotensin-converting enzyme 2 (ACE2) of human respiratory epithelial cells, which leads to infection. Furthermore, low-dose radiation has been found to reduce inflammation and aid the curing of COVID-19. The receptor binding domain (RBD), a recombinant spike protein with a His tag at the C-terminus, binds to ACE2 in human body. A radioiodinated RBD was thus constructed as a molecule-targeted probe to non-invasively explore ACE2 expression *in vivo*, and to investigate radiotherapy pathway for inhibiting ACE2. RBD was labeled with [^{124}I]NaI

using an N-bromosuccinimide (NBS)-mediated method, and ^{124}I-RBD was obtained after purification with a specific activity of 28.9 GBq/nmol. Its radiochemical purity was (RCP) over 90% in saline for 5 days. The dissociation constant of ^{124}I-RBD binding to hACE2 was 75.7 nM. The uptake of ^{124}I-RBD by HeLa^{ACE+} cells at 2 h was 2.96% ± 0.35%, which could be substantially blocked by an excessive amount of RBD, and drop to 1.71% ± 0.23%. In BALB/c mice, the biodistribution of ^{124}I-RBD after intravenous injection showed a moderate metabolism rate, and its 24 h-post injection (p.i.) organ distribution was similar to the expression profile in body. Micro-PET imaging of mice after intrapulmonary injection showed high uptake of lung at 1, 4, 24 h p.i.. In conclusion, the experimental results demonstrate the potential of ^{124}I-RBD as a novel targeted molecular probe for COVID-19. This probe may be used for non-invasive ACE2 mapping in mammals.

Reference

https://www.nature.com/articles/s41401-021-00809-y

ACE2-like carboxypeptidase B38-CAP protects from SARS-CoV-2-induced lung injury

Abstract

Angiotensin-converting enzyme 2 (ACE2) is a receptor for cell entry of SARS-CoV-2, and recombinant soluble ACE2 protein inhibits SARS-CoV-2 infection as a decoy. ACE2 is a carboxypeptidase that degrades angiotensin II, thereby improving the pathologies of cardiovascular disease or acute lung injury. Here it was shown that B38-CAP, an ACE2-like enzyme, is protective against SARS-CoV-2-induced lung injury. Endogenous ACE2 expression is downregulated in the lungs of SARS-CoV-2-infected hamsters, leading to elevation of angiotensin II levels. Recombinant Spike also downregulates ACE2 expression and worsens the symptoms of acid-induced lung injury. B38-CAP does not neutralize cell entry of SARS-CoV-2. However, B38-CAP treatment improves the pathologies of Spike-augmented acid-induced lung injury. In SARS-CoV-2-infected hamsters or human ACE2 transgenic mice, B38-CAP significantly improves lung edema and pathologies of lung injury. These results provide the first *in vivo* evidence that

increasing ACE2-like enzymatic activity is a potential therapeutic strategy to alleviate lung pathologies in COVID-19 patients.

Reference

https://www.nature.com/articles/s41467-021-27097-8

Neurological complications and infection mechanism of SARS-COV-2

Abstract

Currently, SARS-CoV-2 has caused a global pandemic and threatened many lives. Although SARS-CoV-2 mainly causes respiratory diseases, growing data indicate that SARS-CoV-2 can also invade the central nervous system (CNS) and peripheral nervous system (PNS) causing multiple neurological diseases, such as encephalitis, encephalopathy, Guillain-Barré syndrome, meningitis, and skeletal muscular symptoms. Despite the increasing incidences of clinical neurological complications of SARS-CoV-2, the precise neuroinvasion mechanisms of SARS-CoV-2 have not been fully established. In this review, we primarily describe the clinical neurological complications associated with SARS-CoV-2 and discuss the potential mechanisms through which SARS-CoV-2 invades the brain based on the current evidence. Finally, it was summarized the experimental models were used to study SARS-CoV-2 neuroinvasion. These data form the basis for studies on the significance of SARS-CoV-2 infection in the brain.

Reference

https://www.nature.com/articles/s41392-021-00818-7

A COVID-19 peptide vaccine for the induction of SARS-CoV-2 T cell immunity

Abstract

T cell immunity is central for the control of viral infections. CoVac-1 is a peptide-based vaccine candidate, composed of SARS-CoV-2 T cell epitopes derived from various viral proteins, combined with the Toll-like receptor 1/2 agonist XS15 emulsified in Montanide ISA51 VG, aiming to induce profound SARS-CoV-2 T cell immunity to combat COVID-19. A phase I open-label trial was conducted, recruiting 36 participants aged 18 to 80 years, who received one single subcutaneous CoVac-1 vaccination. The primary endpoint was safety analysed until day 56. Immunogenicity in terms of CoVac-1-

induced T-cell response was analysed as main secondary endpoint until day 28 and in the follow-up until month 3. No serious adverse events and no grade 4 adverse events were observed. Expected local granuloma formation was observed in all study subjects, while systemic reactogenicity was absent or mild. SARS-CoV-2-specific T cell responses targeting multiple vaccine peptides were induced in all study participants, mediated by multifunctional T-helper 1 CD4+ and CD8+ T cells. CoVac-1-induced interferon-γ T cell responses persisted in the follow-up analyses and surpassed those detected after SARS-CoV-2 infection as well as after vaccination with approved vaccines. Furthermore, vaccine-induced T- cell responses were unaffected by current SARS-CoV-2 variants of concern (VOC). Together, CoVac-1 showed a favourable safety profile and induced broad, potent and VOC-independent T- cell responses, supporting the presently ongoing evaluation in a phase II trial for patients with B cell/antibody deficiency.

Reference

https://www.nature.com/articles/s41586-021-04232-5

Anti-SARS-CoV-2 antibodies elicited by COVID-19mRNA vaccine exhibit a unique glycosylation pattern

Abstract

Messenger RNA-based vaccines against COVID-19 induce a robust anti-SARS-CoV-2 antibody response with potent viral neutralization activity. Antibody effector functions is determined by its constant region subclasses as well as by its glycosylation patterns, but their role in vaccine efficacy is unclear. Moreover, whether vaccination induces antibodies similar to those in patients with COVID-19 remains unknown. We analyze BNT162b2 vaccine-induced IgG subclass distribution and Fc glycosylation patterns and their potential to drive effector function via Fc-gamma receptors and complement pathways. We identify unique and dynamic pro-inflammatory Fc compositions that are distinct from those in patients with COVID-19 and convalescences. Vaccine-induced anti-spike IgG is characterized by distinct Fab- and Fc-mediated functions between different age groups and in comparison to antibodies generated during natural viral infection. These data highlight the heterogeneity of Fc responses to SARS-CoV-2

infection and vaccination and suggest that they support long-lasting protection differently.

Reference

https://www.cell.com/cell-reports/fulltext/S2211-1247(21)01608-9

Two-adjuvant multiantigen candidate vaccine induces superior protective immune responses against SARS-CoV-2 challenge

Abstract

An ideal vaccine against SARS-CoV-2 is expected to elicit broad immunity to prevent viral infection and disease, with efficient viral clearance in the upper respiratory tract (URT). Here, the N protein and prefusion-full S protein (SFLmut) are combined with flagellin (KF) and cyclic GMP-AMP (cGAMP) to generate a candidate vaccine, and this vaccine elicits stronger systemic and mucosal humoral immunity than vaccines containing other forms of the S protein. Furthermore, the candidate vaccine administered via intranasal route can enhance local immune responses in the respiratory tract. Importantly, human ACE2 transgenic mice given the candidate vaccine are protected against lethal SARS-CoV-2 challenge, with superior protection in the URT compared with that in mice immunized with an inactivated vaccine. In summary, the developed vaccine can elicit a multifaceted immune response and induce robust viral clearance in the URT, which make it a potential vaccine for preventing disease and infection of SARS-CoV-2.

Reference

https://www.cell.com/cell-reports/fulltext/S2211-1247(21)01606-5

Publication Date: Nov 22, 2021

Spike protein multiorgan tropism suppressed by antibodies targeting SARS-CoV-2

Abstract

While there is SARS-CoV-2 multiorgan tropism in severely infected COVID-19 patients, it’s unclear if this occurs in healthy young individuals. In addition, for antibodies that

target the spike protein (SP), it's unclear if these reduce SARS-CoV-2/SP multiorgan tropism equally. Fluorescently labeled SP-NIRF was used to study viral behavior, using an in vivo dynamic imaging system and ex in vivo tissue analysis, in young mice. A SP body-wide biodistribution was found followed by a slow regional elimination, except for the liver, which showed an accumulation. SP uptake was highest for the lungs, and this was followed by kidney, heart and liver, but, unlike the choroid plexus, it was not detected in the brain parenchyma or CSF. Thus, the brain vascular barriers were effective in restricting the entry of SP into brain parenchyma in young healthy mice. While both anti-ACE2 and anti-SP antibodies suppressed SP biodistribution and organ uptake, anti-SP antibody was more effective. By extension, our data support the efficacy of these antibodies on SARS-CoV-2 multiorgan tropism, which could determine COVID-19 organ-specific outcomes.

Reference

https://www.nature.com/articles/s42003-021-02856-x

Long-term sequelae are highly prevalent one year after hospitalization for severe COVID-19

Abstract

Many coronavirus disease 2019 (Covid-19) survivors show symptoms months after acute illness. The aim of this work is to describe the clinical evolution of Covid-19, one year after discharge. A prospective cohort study was performed on 238 patients previously hospitalized for Covid-19 pneumonia in 2020 who already underwent clinical follow-up 4 months post-Covid-19. 200 consented to participate to a 12-months clinical assessment, including: pulmonary function tests with diffusing lung capacity for carbon monoxide (DLCO); post-traumatic stress (PTS) symptoms evaluation by the Impact of Event Scale (IES); motor function evaluation (by Short Physical Performance Battery and 2 min walking test); chest Computed Tomography (CT). After 366 [363–369] days, 79 patients (39.5%) reported at least one symptom. A DLCO < 80% was observed in 96 patients (49.0%). Severe DLCO impairment (< 60%) was reported in 20 patients (10.2%), related to extent of CT scan abnormalities. Some degree of motor impairment was observed in 25.8% of subjects. 37/200 patients (18.5%) showed moderate-to-severe PTS symptoms. In the time elapsed from 4 to 12 months after hospital

discharge, motor function improves, while respiratory function does not, being accompanied by evidence of lung structural damage. Symptoms remain highly prevalent one year after acute illness.

Reference

https://www.nature.com/articles/s41598-021-01215-4

High-resolution epitope mapping and characterization of SARS-CoV-2 antibodies in large cohorts of subjects with COVID-19

Abstract

As Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) continues to spread, characterization of its antibody epitopes, emerging strains, related coronaviruses, and even the human proteome in naturally infected patients can guide the development of effective vaccines and therapies. Since traditional epitope identification tools are dependent upon pre-defined peptide sequences, they are not readily adaptable to diverse viral proteomes. The Serum Epitope Repertoire Analysis (SERA) platform leverages a high diversity random bacterial display library to identify proteome-independent epitope binding specificities which are then analyzed in the context of organisms of interest. When evaluating immune response in the context of SARS-CoV-2, we identify dominant epitope regions and motifs which demonstrate potential to classify mild from severe disease and relate to neutralization activity. We highlight SARS-CoV-2 epitopes that are cross-reactive with other coronaviruses and demonstrate decreased epitope signal for mutant SARS-CoV-2 strains. Collectively, the evolution of SARS-CoV-2 mutants towards reduced antibody response highlight the importance of data-driven development of the vaccines and therapies to treat COVID-19.

Reference

https://www.nature.com/articles/s42003-021-02835-2

Saliva is superior over nasopharyngeal swab for detecting SARS-CoV2 in COVID-19 patients

Abstract

Scaling up of diagnostic capacity is needed to mitigate the global pandemic of SARS-CoV2. However, there are challenges including shortage of sample collection swabs and transport medium. Saliva has been recommended as a simple, low-cost, non-invasive option. However, data from different populations and settings are limited. Here, we showed that saliva could be a good alternative sample to diagnose COVID-19 patients. Pair of NPS-saliva samples was collected from 152 symptomatic; confirmed COVID-19 patients, and compared their positivity rate, viral load, and duration of viral shedding. From 152 patients, 80 (52.63%) tested positive and 72 (47.37%) were negative for SARSA-CoV2 in NPS sample. In saliva, 129 (92.14%) were tested positive and 11 (7.86%) were negative on the day of admission to hospital. The overall percent agreement of RT-PCR result of Saliva to NPS was 70% (196/280). A comparison of viral load from 72 NPS-saliva pair samples on day of admission shows saliva contains significantly higher viral load ($P < 0.001$). In conclusion, saliva has higher yield in detecting SARS-CoV2, and COVID-19 patients show higher viral load and prolonged period of viral shedding in saliva. Therefore, we recommend saliva as a better alternative sample to NPS to diagnose COVID-19 patients.

Reference

https://www.nature.com/articles/s41598-021-02097-2

Publication Date: Nov 20, 2021

Development and characterization of a quantitative ELISA to detect anti-SARS-CoV-2 spike antibodies

Abstract

A novel clinical assay for the detection and quantitation of antibodies against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was adapted from an in-house, research-based enzyme-linked immunosorbent assay (ELISA). Development and validation were performed under regulatory guidelines, and the test obtained emergency use authorization (EUA) from the New York State Department of Health

(NYSDOH) and the Food and Drug Administration (FDA). The Mount Sinai COVID-19 antibody assay is an orthogonal, quantitative direct ELISA test which detects antibodies reactive to the receptor binding domain (RBD) and the spike protein of the novel SARS-CoV-2. The assay is performed on 96-well plates coated with either SARS-CoV-2 recombinant RBD or spike proteins. The test is divided into two stages, a qualitative screening assay against RBD and a quantitative assay against the full-length spike protein. The test uses pooled high titer serum as a reference standard. Negative pre-COVID-19 and positive post-COVID-19, PCR-confirmed specimens were incorporated in each ELISA test run, and the assays were performed independently at two different locations.

The Mount Sinai COVID-19 serology performed with high sensitivity and specificity, 92.5% (95% CI: 0.785 – 0.980) and 100% (CI: 0.939 – 1.000) respectively. Between-run precision was assessed with a single run repeated over 22 days; and within-run precision was assessed with 10 replicates per day over 22 days. Both were within reported acceptance criteria (CV ≤20%).

This population-based study reveals the applicability and reliability of this novel orthogonal COVID-19 serology test for the detection and quantitation of antibodies against SARS-CoV-2, allowing a broad set of clinical applications, including the broad evaluation of SARS-CoV-2 seroprevalence and antibody profiling in different population subsets.

Reference

https://www.cell.com/heliyon/fulltext/S2405-8440(21)02547-0

Publication Date: Nov 19, 2021

A method for the identification of COVID-19 biomarkers in human breath using Proton Transfer Reaction Time-of-Flight Mass Spectrometry

Abstract

Background: COVID-19 has caused a worldwide pandemic, making the early detection of the virus crucial. An approach was presented for the determination of COVID-19 infection based on breath analysis.

Methods: A high sensitivity mass spectrometer was combined with artificial intelligence and used to develop a method for the identification of COVID-19 in human breath within seconds. A set of 1137 positive and negative subjects from different age groups, collected in two periods from two hospitals in the USA, from 26 August, 2020 until 15 September, 2020 and from 11 September, 2020 until 11 November, 2020, was used for the method development. The subjects exhaled in a Tedlar bag, and the exhaled breath samples were subsequently analyzed using a Proton Transfer Reaction Time-of-Flight Mass Spectrometer (PTR-ToF-MS). The produced mass spectra were introduced to a series of machine learning models. 70% of the data was used for these sub-models' training and 30% was used for testing.

Findings: A set of 340 samples, 95 positives and 245 negatives, was used for the testing. The combined models successfully predicted 77 out of the 95 samples as positives and 199 out of the 245 samples as negatives. The overall accuracy of the model was 81.2%. Since over 50% of the total positive samples belonged to the age group of over 55 years old, the performance of the model in this category was also separately evaluated on 339 subjects (170 negative and 169 positive). The model correctly identified 166 out of the 170 negatives and 164 out of the 169 positives. The model accuracy in this case was 97.3%.

Interpretation: The results showed that this method for the identification of COVID-19 infection is a promising tool, which can give fast and accurate results.

Reference

https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00488-0/fulltext

Ecology, evolution and spillover of coronaviruses from bats

Abstract

In the past two decades, three coronaviruses with ancestral origins in bats have emerged and caused widespread outbreaks in humans, including severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Since the first SARS epidemic in 2002–2003, the appreciation of bats as key hosts of zoonotic coronaviruses has advanced rapidly. More than 4,000 coronavirus sequences from 14 bat families have been identified, yet the true diversity of bat coronaviruses is probably much greater.

Given that bats are the likely evolutionary source for several human coronaviruses, including strains that cause mild upper respiratory tract disease, their role in historic and future pandemics requires ongoing investigation. Information on bat–coronavirus interactions was reviewed and integrated at the molecular, tissue, host and population levels. Critical gaps in knowledge of bat coronaviruses were identified, which relate to spillover and pandemic risk, including the pathways to zoonotic spillover, the infection dynamics within bat reservoir hosts, the role of prior adaptation in intermediate hosts for zoonotic transmission and the viral genotypes or traits that predict zoonotic capacity and pandemic potential. Filling these knowledge gaps may help prevent the next pandemic.

Reference

https://www.nature.com/articles/s41579-021-00652-2

Large scale discovery of coronavirus-host factor protein interaction motifs reveals SARS-CoV-2 specific mechanisms and vulnerabilities

Abstract

Viral proteins make extensive use of short peptide interaction motifs to hijack cellular host factors. However, most current large-scale methods do not identify this important class of protein-protein interactions. Uncovering peptide mediated interactions provides both a molecular understanding of viral interactions with their host and the foundation for developing novel antiviral reagents. Here a viral peptide discovery approach was described covering 23 coronavirus strains that provides high resolution information on direct virus-host interactions. 269 Peptide-based interactions were identified for 18 coronaviruses including a specific interaction between the human G3BP1/2 proteins and an ΦxFG peptide motif in the SARS-CoV-2 nucleocapsid (N) protein. This interaction supports viral replication and through its ΦxFG motif N rewires the G3BP1/2 interactome to disrupt stress granules. A peptide-based inhibitor disrupting the G3BP1/2-N interaction dampened SARS-CoV-2 infection showing that our results can be directly translated into novel specific antiviral reagents.

Reference

https://www.nature.com/articles/s41467-021-26498-z

Investigation of SARS-CoV-2 inactivation using UV-C LEDs in public environments via ray-tracing simulation

Abstract

This paper proposes an investigating SARS-CoV-2 inactivation on surfaces with UV-C LED irradiation using our in-house-developed ray-tracing simulator. The results are benchmarked with experiments and Zemax OpticStudio commercial software simulation to demonstrate our simulator's easy accessibility and high reliability. The tool can input the radiant profile of the flexible LED source and accurately yield the irradiance distribution emitted from an LED-based system in 3D environments. The UV-C operating space can be divided into the safe, buffer, and germicidal zones for setting up a UV-C LED system. Based on the published measurement data, the level of SARS-CoV-2 inactivation has been defined as a function of UV-C irradiation. A realistic case of public space, i.e., a food court in Singapore, has been numerically investigated to demonstrate the relative impact of environmental UV-C attenuation on the SARS-CoV-2 inactivation. We optimise a specific UV-C LED germicidal system and its corresponding exposure time according to the simulation results. These ray-tracing-based simulations provide a useful guideline for safe deployment and efficient design for germicidal UV-C LED technology.

Reference

https://www.nature.com/articles/s41598-021-02156-8

Comparison of ROX and HACOR scales to predict high-flow nasal cannula failure in patients with SARS-CoV-2 pneumonia

Abstract

The pandemic of SARSCov2 infection has created a challenge in health services worldwide. Some scales have been applied to evaluate the risk of intubation, such as the ROX and HACOR. The objective of this study is to compare the predictive capacity of the HACOR scale and the ROX index and define the optimal cut-off points. Study of diagnostic tests based on a retrospective cohort. Composite outcome was the proportion of patients that needed endotracheal intubation (ETI) or died of COVID19 pneumonia. Discrimination capacity was compared by the area under the curve of each

of the two scales and the optimal cut-off point was determined using the Liu method. 245 patients were included, of which 140 (57%) required ETI and 152 (62%) had the composite end result of high-flow nasal cannula (HFNC) failure. The discrimination capacity was similar for the two scales with an area under receiver operating characteristic curve of 0.71 and 0.72 for the HACOR scale for the ROX index, respectively. The optimal cut-off point for the ROX index was 5.6 (sensitivity 62% specificity 65%), while the optimal cut-off point for the HACOR scale was 5.5 (sensitivity 66% specificity 65%). The HACOR scale and the ROX index have a moderate predictive capacity to predict failures to the HFNC strategy. They can be used in conjunction with other clinical variables to define which patients may require invasive mechanical ventilation.

Reference

https://www.nature.com/articles/s41598-021-02078-5

Controlling long-term SARS-CoV-2 infections can slow viral evolution and reduce the risk of treatment failure

Abstract

The rapid emergence and expansion of novel SARS-CoV-2 variants threatens our ability to achieve herd immunity for COVID-19. These novel SARS-CoV-2 variants often harbor multiple point mutations, conferring one or more evolutionarily advantageous traits, such as increased transmissibility, immune evasion and longer infection duration. In a number of cases, variant emergence has been linked to long-term infections in individuals who were either immunocompromised or treated with convalescent plasma. In this paper, we used a stochastic evolutionary modeling framework to explore the emergence of fitter variants of SARS-CoV-2 during long-term infections. We found that increased viral load and infection duration favor emergence of such variants. While the overall probability of emergence and subsequent transmission from any given infection is low, on a population level these events occur fairly frequently. Targeting these low-probability stochastic events that lead to the establishment of novel advantageous viral variants might allow us to slow the rate at which they emerge in the patient population, and prevent them from spreading deterministically due to natural selection. The work

thus suggests practical ways to achieve control of long-term SARS-CoV-2 infections, which will be critical for slowing the rate of viral evolution.

Reference

https://www.nature.com/articles/s41598-021-02148-8

Pannexin-1 channel opening is critical for COVID-19 pathogenesis

Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) rapidly rampaged worldwide, causing a pandemic of coronavirus disease (COVID -19), but the biology of SARS-CoV-2 is under investigation. We demonstrate that both SARS-CoV-2 spike protein and human coronavirus 229E (hCoV-229E) or its purified S protein, one of the main viruses responsible for the common cold, induce the transient opening of Pannexin-1 (Panx-1) channels in human lung epithelial cells. However, the Panx-1 channel opening induced by SARS-CoV-2 is greater and more prolonged than hCoV-229E/S protein, resulting in ATP, PGE2, and IL-1β release. Analysis of lung lavage and tissues indicate that Panx-1 mRNA expression is associated with increased ATP, PGE2, and IL-1β levels. Panx-1 channel opening induced by SARS-CoV-2 spike protein is angiotensin-converting enzyme 2 (ACE-2), endocytosis, and furin dependent. Overall, we demonstrated that Panx-1 is a critical contributor to SARS-CoV-2 infection and should be considered an alternative therapy.

Reference

https://www.cell.com/iscience/fulltext/S2589-0042(21)01449-8

COVID-19 genetic risk variants are associated with expression of multiple genes in diverse immune cell types

Abstract

Common genetic polymorphisms associated with COVID-19 illness can be utilized for discovering molecular pathways and cell types driving disease pathogenesis. Given the importance of immune cells in the pathogenesis of COVID-19 illness, here the effects of COVID-19-risk variants were assessed on gene expression in a wide range of immune cell types. Transcriptome-wide association study and colocalization analysis revealed

putative causal genes and the specific immune cell types where gene expression is most influenced by COVID-19-risk variants. Notable examples include OAS1 in non-classical monocytes, DTX1 in B cells, IL10RB in NK cells, CXCR6 in follicular helper T cells, CCR9 in regulatory T cells and ARL17A in TH2 cells. By analysis of transposase accessible chromatin and H3K27ac-based chromatin-interaction maps of immune cell types, potentially functional COVID-19-risk variants were prioritized. The study highlights the potential of COVID-19 genetic risk variants to impact the function of diverse immune cell types and influence severe disease manifestations.

Reference

https://www.nature.com/articles/s41467-021-26888-3

Publication Date: Nov 18, 2021

Current and future nanoparticle vaccines for COVID-19

Abstract

COVID-19 has become a major cause of global mortality and driven massive health and economic disruptions. Mass global vaccination offers the most efficient pathway towards ending the pandemic. The development and deployment of first-generation COVID-19 vaccines, encompassing mRNA or viral vectors, has proceeded at a phenomenal pace. Going forward, nanoparticle-based vaccines which deliver SARS-CoV-2 antigens will play an increasing role in extending or improving vaccination outcomes against COVID-19. At present, over 26 nanoparticle vaccine candidates have advanced into clinical testing, with ~60 more in pre-clinical development. Here, the emerging promise of nanotechnology in vaccine design and manufacturing was discussed to combat SARS-CoV-2, and highlight opportunities and challenges presented by these novel vaccine platforms.

Reference

https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(21)00493-X/fulltext

Development of COVID-19 vaccine using a dual Toll-like receptor ligand liposome adjuvant

Abstract

A SARS-CoV-2 spike subunit vaccine formulation was developed containing dual TLR ligand liposome adjuvant. The vaccine-induced robust systemic neutralizing antibodies and completely protected mice from a lethal challenge. Two immunizations protected against lung injury and cleared the virus from lungs upon challenge. The adjuvanted vaccine also elicited systemic and local anti-Spike IgA which can be an important feature for a COVID-19 vaccine.

Reference

https://www.nature.com/articles/s41541-021-00399-0

Multifactorial seroprofiling dissects the contribution of pre-existing human coronaviruses responses to SARS-CoV-2 immunity

Abstract

Determination of SARS-CoV-2 antibody responses in the context of pre-existing immunity to circulating human coronavirus (HCoV) is critical for understanding protective immunity. Here we perform a multifactorial analysis of SARS-CoV-2 and HCoV antibody responses in pre-pandemic (N = 825) and SARS-CoV-2-infected donors (N = 389) using a custom-designed multiplex ABCORA assay. ABCORA seroprofiling, when combined with computational modeling, enables accurate definition of SARS-CoV-2 seroconversion and prediction of neutralization activity, and reveals intriguing interrelations with HCoV immunity. Specifically, higher HCoV antibody levels in SARS-CoV-2-negative donors suggest that pre-existing HCoV immunity may provide protection against SARS-CoV-2 acquisition. In those infected, higher HCoV activity is associated with elevated SARS-CoV-2 responses, indicating cross-stimulation. Most importantly, HCoV immunity may impact disease severity, as patients with high HCoV reactivity are less likely to require hospitalization. Collectively, our results suggest that HCoV immunity may promote rapid development of SARS-CoV-2-specific immunity, thereby underscoring the importance of exploring cross-protective responses for comprehensive coronavirus prevention.

Reference

https://www.nature.com/articles/s41467-021-27040-x

Comparative analysis of loop-mediated isothermal amplification (LAMP)-based assays for rapid detection of SARS-CoV-2 genes

Abstract

The COVID-19 pandemic caused by SARS-CoV-2 has infected millions worldwide, therefore there is an urgent need to increase our diagnostic capacity to identify infected cases. Although RT-qPCR remains the gold standard for SARS-CoV-2 detection, this method requires specialised equipment in a diagnostic laboratory and has a long turn-around time to process the samples. To address this, several groups have recently reported the development of loop-mediated isothermal amplification (LAMP) as a simple, low cost and rapid method for SARS-CoV-2 detection. Herein we present a comparative analysis of three LAMP-based assays that target different regions of the SARS-CoV-2: ORF1ab RdRP, ORF1ab nsp3 and Gene N. We perform a detailed assessment of their sensitivity, kinetics and false positive rates for SARS-CoV-2 diagnostics in LAMP or RT-LAMP reactions, using colorimetric or fluorescent detection. Our results independently validate that all three assays can detect SARS-CoV-2 in 30 min, with robust accuracy at detecting as little as 1000 RNA copies and the results can be visualised simply by color changes. Incorporation of RT-LAMP with fluorescent detection further increases the detection sensitivity to as little as 100 RNA copies. We also note the shortcomings of some LAMP-based assays, including variable results with shorter reaction time or lower load of SARS-CoV-2, and false positive results in some experimental conditions and clinical saliva samples. Overall for RT-LAMP detection, the ORF1ab RdRP and ORF1ab nsp3 assays have faster kinetics for detection but varying degrees of false positives detection, whereas the Gene N assay exhibits no false positives in 30 min reaction time, which highlights the importance of optimal primer design to minimise false-positives in RT-LAMP. This study provides validation of the performance of LAMP-based assays as a rapid, highly sensitive detection method for SARS-CoV-2, which have important implications in development of point-of-care diagnostics for SARS-CoV-2.

Reference

https://www.nature.com/articles/s41598-021-01472-3

Allelic variation in class I HLA determines CD8+ T cell repertoire shape and cross-reactive memory responses to SARS-CoV-2

Abstract

Effective presentation of antigens by HLA class I molecules to CD8+ T cells is required for viral elimination and generation of long-term immunological memory. In this study, we applied a single-cell, multi-omic technology to generate a unified ex vivo characterization of the CD8+ T cell response to SARS-CoV-2 across 4 major HLA class I alleles. We found that HLA genotype conditions key features of epitope specificity, TCR α/β sequence diversity, and the utilization of pre-existing SARS-CoV-2 reactive memory T cell pools. Single-cell transcriptomics revealed functionally diverse T cell phenotypes of SARS-CoV-2-reactive T cells, associated with both disease stage and epitope specificity. The results show that HLA variations significantly influence the CD8+ T cell repertoire shape and utilization of immune recall upon SARS-CoV-2 infection.

Reference

https://www.science.org/doi/10.1126/sciimmunol.abk3070

Population impact of SARS-CoV-2 variants with enhanced transmissibility and/or partial immune escape

Abstract

SARS-CoV-2 variants of concern exhibit varying degrees of transmissibility and, in some cases, escape from acquired immunity. Much effort has been devoted to measuring these phenotypes, but understanding their impact on the course of the pandemic – especially that of immune escape – has remained a challenge. Here, a mathematical model was used to simulate the dynamics of wildtype and variant strains of SARS-CoV-2 in the context of vaccine rollout and nonpharmaceutical interventions. It was shown that variants with enhanced transmissibility frequently increase epidemic severity, whereas those with partial immune escape either fail to spread widely, or primarily cause reinfections and breakthrough infections. However, when these phenotypes are combined, a variant can continue spreading even as immunity builds up

in the population, limiting the impact of vaccination and exacerbating the epidemic. These findings help explain the trajectories of past and present SARS-CoV-2 variants and may inform variant assessment and response in the future.

Reference

https://www.cell.com/cell/fulltext/S0092-8674(21)01374-X

REPORT

Publication Date: Nov 19, 2021

Nosocomial COVID-19 infection mortality following surgery for severe progressive cervical myelopathy: A case report

Introduction: The unique case of a nosocomial COVID infection acquired after urgent surgical intervention for cervical myelopathy, as well as the sequelae that followed in the postoperative period, was presented.

Case presentation: An initially COVID-negative patient underwent urgent surgical intervention for cervical myelopathy with significant neurological deterioration. She underwent an uncomplicated staged anterior cervical discectomy and fusion with corpectomy, as well as a subsequent posterior cervical instrumented fusion within the same hospitalization. The patient would refuse to adhere to standard COVID precautions during her admission and demonstrated rapid decompensation following her particularly uneventful surgeries, ultimately leading to her expiration. A laboratory test confirmed that she had contracted COVID at the time of the patient's death.

Discussion: This report highlights the repercussions of COVID-19 infection during the perioperative period and its implications on surgical outcomes. The stresses of surgery and the body's immunosuppressive responses during this time place patients at particular risk for the contraction of this virus. The standard precautions should be followed and vaccination should be considered for surgical candidates prior to their operations, as they become more readily accessible.

Reference

https://www.nature.com/articles/s41394-021-00465-8

COMMENT

Publication Date: Nov 19, 2021

COVID-19 vaccination and cancer immunotherapy: Should they stick together?

The combination of COVID-19 vaccination with immunotherapy by checkpoint inhibitors in cancer patients could intensify immunological stimulation with potential reciprocal benefits. Here, more closely the possible adverse events were examined that can arise in each treatment modality. The conclusion is that caution should be exercised when combining both treatments.

Reference

https://www.nature.com/articles/s41416-021-01618-0