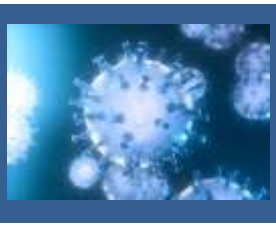
COVID-19

Oct 28 – Nov 03, 2021



RESEARCH PUBLICATIONS

Publication Date: Nov 03, 2021

Identification of LZTFL1 as a candidate effector gene at a COVID-19 risk locus

Abstract

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) disease (COVID-19) pandemic has caused millions of deaths worldwide. Genome-wide association studies identified the 3p21.31 region as conferring a twofold increased risk of respiratory failure. Here, using a combined multiomics and machine learning approach, we identify the gain-of-function risk A allele of an SNP, rs17713054G>A, as a probable causative variant. We show with chromosome conformation capture and gene-expression analysis that the rs17713054-affected enhancer upregulates the interacting gene, leucine zipper transcription factor like 1 (LZTFL1). Selective spatial transcriptomic analysis of lung biopsies from patients with COVID-19 shows the presence of signals associated with epithelial–mesenchymal transition (EMT), a viral response pathway that is regulated by LZTFL1. We conclude that pulmonary epithelial cells undergoing EMT, rather than immune cells, are likely responsible for the 3p21.31-associated risk. Since the 3p21.31 effect is conferred by a gain-of-function, LZTFL1 may represent a therapeutic target.

Reference

https://www.nature.com/articles/s41588-021-00955-3

Infection induced SARS-CoV-2 seroprevalence and heterogeneity of antibody responses in a general population cohort study in Catalonia Spain

Abstract

Sparse data exist on the complex natural immunity to SARS-CoV-2 at the population level. We applied a well-validated multiplex serology test in 5000 participants of a general population study in Catalonia in blood samples collected from end June to mid November 2020. Based on responses to fifteen isotype-antigen combinations, we detected a seroprevalence of 18.1% in adults (n = 4740), and modeled extrapolation to the general population of Catalonia indicated a 15.3% seroprevalence. Antibodies persisted up to 9 months after infection. Immune profiling of infected individuals revealed that with increasing severity of infection (asymptomatic, 1–3 symptoms, ≥ 4 symptoms, admitted to hospital/ICU), seroresponses were more robust and rich with a shift towards IgG over IgA and anti-spike over anti-nucleocapsid responses. Among seropositive participants, lower antibody levels were observed for those ≥ 60 years vs < 60 years old and smokers vs non-smokers. Overweight/obese participants vs normal weight had higher antibody levels. Adolescents (13–15 years old) (n = 260) showed a seroprevalence of 11.5%, were less likely to be tested seropositive compared to their parents and had dominant anti-spike rather than anti-nucleocapsid IgG responses. Our study provides an unbiased estimate of SARS-CoV-2 seroprevalence in Catalonia and new evidence on the durability and heterogeneity of post-infection immunity.

Reference

https://www.nature.com/articles/s41598-021-00807-4

Sensing of cytoplasmic chromatin by cGAS activates innate immune response in SARS-CoV-2 infection

Abstract

The global coronavirus disease 2019 (COVID-19) pandemic is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a positive-sense RNA virus. How the host immune system senses and responds to SARS-CoV-2 infection remain largely unresolved. Here, we report that SARS-CoV-2 infection activates the innate immune

response through the cytosolic DNA sensing cGAS-STING pathway. SARS-CoV-2 infection induces the cellular level of 2′3′-cGAMP associated with STING activation. cGAS recognizes chromatin DNA shuttled from the nucleus as a result of cell-to-cell fusion upon SARS-CoV-2 infection. We further demonstrate that the expression of spike protein from SARS-CoV-2 and ACE2 from host cells is sufficient to trigger cytoplasmic chromatin upon cell fusion. Furthermore, cytoplasmic chromatin-cGAS-STING pathway, but not MAVS-mediated viral RNA sensing pathway, contributes to interferon and pro-inflammatory gene expression upon cell fusion. Finally, we show that cGAS is required for host antiviral responses against SARS-CoV-2, and a STING-activating compound potently inhibits viral replication. Together, our study reported a previously unappreciated mechanism by which the host innate immune system responds to SARS-CoV-2 infection, mediated by cytoplasmic chromatin from the infected cells. Targeting the cytoplasmic chromatin-cGAS-STING pathway may offer novel therapeutic opportunities in treating COVID-19. In addition, these findings extend our knowledge in host defense against viral infection by showing that host cells' self-nucleic acids can be employed as a "danger signal" to alarm the immune system.

Reference

https://www.nature.com/articles/s41392-021-00800-3

A non-ACE2 competing human single-domain antibody confers broad neutralization against SARS-CoV-2 and circulating variants

Abstract

The current COVID-19 pandemic has heavily burdened the global public health system and may keep simmering for years. The frequent emergence of immune escape variants have spurred the search for prophylactic vaccines and therapeutic antibodies that confer broad protection against SARS-CoV-2 variants. Here we show that the bivalency of an affinity maturated fully human single-domain antibody (n3113.1-Fc) exhibits exquisite neutralizing potency against SARS-CoV-2 pseudovirus, and confers effective prophylactic and therapeutic protection against authentic SARS-CoV-2 in the host cell receptor angiotensin-converting enzyme 2 (ACE2) humanized mice. The crystal structure of n3113 in complex with the receptor-binding domain (RBD) of SARS-CoV-2, combined with the cryo-EM structures of n3113 and spike ecto-domain, reveals

that n3113 binds to the side surface of up-state RBD with no competition with ACE2. The binding of n3113 to this novel epitope stabilizes spike in up-state conformations but inhibits SARS-CoV-2 S mediated membrane fusion, expanding our recognition of neutralization by antibodies against SARS-CoV-2. Binding assay and pseudovirus neutralization assay show no evasion of recently prevalent SARS-CoV-2 lineages, including Alpha (B.1.1.7), Beta (B.1.351), Gamma (P.1), and Delta (B.1.617.2) for n3113.1-Fc with Y58L mutation, demonstrating the potential of n3113.1-Fc (Y58L) as a promising candidate for clinical development to treat COVID-19.

Reference

https://www.nature.com/articles/s41392-021-00810-1

SARS-CoV-2 IgG seropositivity in a cohort of 449 non-hospitalized individuals during Spanish COVID-19 lockdown

Abstract

The Coronavirus Disease of 2019 (COVID-19) pandemic caused by SARS-CoV-2 led the Spanish government to impose a national lockdown in an attempt to control the spread of the infection. Mobility restrictions and the requirement of a medical prescription for serological testing for COVID-19 were included among the control measures. Under this scenario, between April 15th and June 15th, 2020, we performed an observational study including 449 individuals allowed to be tested according to the governmental restrictions, i.e. fulfilling the following prescription requirements: manifestation of COVID-19-compatible symptoms, contact with a confirmed COVID-19 patient, or employment as an essential worker, including health care workers, firefighters and public safety personnel such as police. Importantly, a relevant feature of the studied cohort was that none of the participants had been hospitalized. We analyzed SARS-CoV-2 IgG seropositivity in this specific cohort, uncovering intrinsic features of great demographic interest. The overall rate of IgG seropositivity was 33.69% (95% CI: 29.27–38.21). This frequency was comparable among the different participant occupations. A RT-PCR positive test, contact with a household member previously tested positive and the presence of COVID-19-compatible symptoms were positively associated with IgG + results. Among these symptoms, ageusia/anosmia was positively and independently associated with SARS-CoV-2 IgG seropositivity, while odynophagia

was inversely associated. However, fever, ageusia/anosmia and asthenia were the most frequent symptoms described by IgG + subjects. Therefore, our data illustrate how specific cohorts display particular characteristics that should be taken into account when studying population-wide SARS-CoV-2 seroprevalence and key defining symptoms of COVID-19.

Reference

https://www.nature.com/articles/s41598-021-00990-4

The associations of previous influenza/upper respiratory infection with COVID-19 susceptibility/morbidity/mortality: A nationwide cohort study in South Korea

Abstract

It was aimed to investigate the associations of previous influenza/URI with the susceptibility of COVID-19 patients compared to that of non-COVID-19 participants. A nationwide COVID-19 cohort database was collected by the Korea National Health Insurance Corporation. A total of 8,070 COVID-19 patients (1 January 2020 through 4 June 2020) were matched with 32,280 control participants. Severe COVID-19 morbidity was defined based on the treatment histories of the intensive care unit, invasive ventilation, and extracorporeal membrane oxygenation and death. The susceptibility/morbidity/mortality associated with prior histories of 1–14, 1–30, 1–90, 15–45, 15–90, and 31–90 days before COVID-19 onset were analyzed using conditional/unconditional logistic regression. Prior influenza infection was related to increased susceptibility to COVID-19 (adjusted odds ratio [95% confidence interval] = 3.07 [1.61–5.85] for 1–14 days and 1.91 [1.54–2.37] for 1–90 days). Prior URI was also associated with increased susceptibility to COVID-19 (6.95 [6.38–7.58] for 1–14 days, 4.99 [4.64–5.37] for 1–30 days, and 2.70 [2.55–2.86] for 1–90 days). COVID-19 morbidity was positively associated with influenza (3.64 [1.55–9.21] and 3.59 [1.42–9.05]) and URI (1.40 [1.11–1.78] and 1.28 [1.02–1.61]) at 1–14 days and 1–30 days, respectively. Overall, previous influenza/URI did not show an association with COVID-19 mortality. Previous influenza/URI histories were associated with increased COVID-19 susceptibility and morbidity. Our findings indicate why controlling influenza/URI is important during the COVID-19 pandemic.

Reference

https://www.nature.com/articles/s41598-021-00428-x

Association between vaccination with the BNT162b2 mRNA COVID-19 vaccine and Bell's palsy: A population-based study

Abstract

Background: An excess risk of Bell's palsy has been suggested after mRNA vaccines. We examined the association between the BNT162b2 mRNA COVID-19 vaccine and Bell's palsy.

Methods: Using the database of the largest healthcare provider in Israel, we retrieved data from different periods in 2018-2021. Observed cases of Bell's palsy occurring within 21-days after the first vaccine dose and within 30-days after the second vaccine dose were compared to the expected cases, based on the experience of the population in 2019. Standardized incidence ratios (SIRs) and attributable risks (ARs) were computed.

Findings: Overall, 132 cases of Bell's palsy were reported in 2,594,990 vaccinees with the first dose, and 152 cases in 2,434,674 vaccinees after the second dose. The age and sex weighted SIRs were 1.36(95% CI, 1.14-1.61) and 1.16(0.99-1.36) after the first and second vaccine dose, respectively. SIRs tended to be higher in older age groups after the first and second vaccine doses. The estimates were more pronounced in older females after the first vaccine dose; SIR=1.71(1.10-2.54) at age 45-64, and 2.51(1.65-3.68) at age ≥65 years. The highest AR was 4.46 per 100,000 vaccinees detected in females aged ≥65 years. In patients with previous history of Bell's palsy, only 4 cases of Bell's palsy were reported in 7,567 vaccinees and 10 cases in 7,045 vaccinees after the first and the second dose, respectively. The age and sex weighted SIRs were 1.15(0.36-2.76) and 2.15(1.09-3.83) after the first and second vaccine dose, respectively.

Interpretation: This study suggests that the BNT162b2 mRNA COVID-19 vaccine might be associated with increased risk of Bell's palsy. The small estimated attributable risks suggest that the impact on public health is relatively minor. The benefits of vaccinations

explicitly outweigh the possible link to Bell's palsy that has high recovery rate if timely treated with corticosteroids.

Reference

https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762(21)00222-2/fulltext

Prevalence and impact of COVID-19 sequelae on treatment and survival of patients with cancer who recovered from SARS-CoV-2 infection: Evidence from the OnCovid retrospective, multicentre registry study

Abstract

Background: The medium-term and long-term impact of COVID-19 in patients with cancer is not yet known. In this study, we aimed to describe the prevalence of COVID-19 sequelae and their impact on the survival of patients with cancer. We also aimed to describe patterns of resumption and modifications of systemic anti-cancer therapy following recovery from SARS-CoV-2 infection.

Methods: OnCovid is an active European registry study enrolling consecutive patients aged 18 years or older with a history of solid or haematological malignancy and who had a diagnosis of RT-PCR confirmed SARS-CoV-2 infection. For this retrospective study, patients were enrolled from 35 institutions across Belgium, France, Germany, Italy, Spain, and the UK. Patients who were diagnosed with SARS-CoV-2 infection between Feb 27, 2020, and Feb 14, 2021, and entered into the registry at the point of data lock (March 1, 2021), were eligible for analysis. The present analysis was focused on COVID-19 survivors who underwent clinical reassessment at each participating institution. We documented prevalence of COVID-19 sequelae and described factors associated with their development and their association with post-COVID-19 survival, which was defined as the interval from post-COVID-19 reassessment to the patients' death or last follow-up. We also evaluated resumption of systemic anti-cancer therapy in patients treated within 4 weeks of COVID-19 diagnosis. The OnCovid study is registered in ClinicalTrials.gov, NCT04393974.

Findings: 2795 Patients diagnosed with SARS-CoV-2 infection between Feb 27, 2020, and Feb 14, 2021, were entered into the study by the time of the data lock on March 1, 2021. After the exclusion of ineligible patients, the final study population consisted of

2634 patients. 1557 COVID-19 survivors underwent a formal clinical reassessment after a median of 22·1 months (IQR 8·4–57·8) from cancer diagnosis and 44 days (28–329) from COVID-19 diagnosis. 234 (15·0%) patients reported COVID-19 sequelae, including respiratory symptoms (116 [49·6%]) and residual fatigue (96 [41·0%]). Sequelae were more common in men (vs women; p=0·041), patients aged 65 years or older (vs other age groups; p=0·048), patients with two or more comorbidities (vs one or none; p=0·0006), and patients with a history of smoking (vs no smoking history; p=0·0004). Sequelae were associated with hospitalisation for COVID-19 (p<0·0001), complicated COVID-19 (p<0·0001), and COVID-19 therapy (p=0·0002). With a median post-COVID-19 follow-up of 128 days (95% CI 113–148), COVID-19 sequelae were associated with an increased risk of death (hazard ratio [HR] 1·80 [95% CI 1·18–2·75]) after adjusting for time to post-COVID-19 reassessment, sex, age, comorbidity burden, tumour characteristics, anticancer therapy, and COVID-19 severity. Among 466 patients on systemic anti-cancer therapy, 70 (15·0%) permanently discontinued therapy, and 178 (38·2%) resumed treatment with a dose or regimen adjustment. Permanent treatment discontinuations were independently associated with an increased risk of death (HR 3·53 [95% CI 1·45–8·59]), but dose or regimen adjustments were not (0·84 [0·35–2·02]).

Interpretation: Sequelae post-COVID-19 affect up to 15% of patients with cancer and adversely affect survival and oncological outcomes after recovery. Adjustments to systemic anti-cancer therapy can be safely pursued in treatment-eligible patients.

Reference

https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(21)00573-8/fulltext

Publication Date: Nov 02, 2021

Anti-inflammatory adipokines: Chemerin, vaspin, omentin concentrations and SARS-CoV-2 outcomes

Abstract

Coronavirus disease 2019 (COVID-19) is associated with systemic inflammation. A wide range of adipokines activities suggests they influence pathogenesis and infection course. The aim was to assess concentrations of chemerin, omentin, and vaspin among

COVID-19 patients with an emphasis on adipokines relationship with COVID-19 severity, concomitant metabolic abnormalities and liver dysfunction. Serum chemerin, omentin and vaspin concentrations were measured in serum collected from 70 COVID-19 patients at the moment of admission to hospital, before any treatment was applied and 20 healthy controls. Serum chemerin and omentin concentrations were significantly decreased in COVID-19 patients compared to healthy volunteers (271.0 vs. 373.0 ng/ml; $p < 0.001$ and 482.1 vs. 814.3 ng/ml; $p = 0.01$, respectively). There were no correlations of analyzed adipokines with COVID-19 severity based on the presence of pneumonia, dyspnea, or necessity of Intensive Care Unit hospitalization (ICU). Liver test abnormalities did not influence adipokines levels. Elevated GGT activity was associated with ICU admission, presence of pneumonia and elevated concentrations of CRP, ferritin and interleukin 6. Chemerin and omentin depletion in COVID-19 patients suggests that this adipokines deficiency play influential role in disease pathogenesis. However, there was no relationship between lower adipokines level and frequency of COVID-19 symptoms as well as disease severity. The only predictive factor which could predispose to a more severe COVID-19 course, including the presence of pneumonia and ICU hospitalization, was GGT activity.

Reference

https://www.nature.com/articles/s41598-021-00928-w

Potent SARS-CoV-2 neutralizing antibodies with protective efficacy against newly emerged mutational variants

Abstract

Since severe a Accumulating mutations in the SARS-CoV-2 Spike (S) protein can increase the possibility of immune escape, challenging the present COVID-19 prophylaxis and clinical interventions. Here, 3 receptor binding domain (RBD) specific monoclonal antibodies (mAbs), 58G6, 510A5 and 13G9, with high neutralizing potency blocking authentic SARS-CoV-2 virus display remarkable efficacy against authentic B.1.351 virus. Surprisingly, structural analysis has revealed that 58G6 and 13G9 both recognize the steric region $S^{470–495}$ on the RBD, overlapping the E484K mutation presented in B.1.351. Also, 58G6 directly binds to another region $S^{450–458}$ in the RBD. Significantly, 58G6 and 510A5 both demonstrate prophylactic efficacy against authentic

SARS-CoV-2 and B.1.351 viruses in the transgenic mice expressing human ACE2 (hACE2), protecting weight loss and reducing virus loads. Together, we have evidenced 2 potent neutralizing Abs with unique mechanism targeting authentic SARS-CoV-2 mutants, which can be promising candidates to fulfill the urgent needs for the prolonged COVID-19 pandemic.

Reference

https://www.nature.com/articles/s41467-021-26539-7

Screening HLA-A-restricted T cell epitopes of SARS-CoV-2 and the induction of CD8+ T cell responses in HLA-A transgenic mice

Abstract

Since severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2)-specific T cells have been found to play essential roles in host immune protection and pathology in patients with coronavirus disease 2019 (COVID-19), this study focused on the functional validation of T cell epitopes and the development of vaccines that induce specific T cell responses. A total of 120 CD8+ T cell epitopes from the E, M, N, S, and RdRp proteins were functionally validated. Among these, 110, 15, 6, 14, and 12 epitopes were highly homologous with SARS-CoV, OC43, NL63, HKU1, and 229E, respectively; in addition, four epitopes from the S protein displayed one amino acid that was distinct from the current SARS-CoV-2 variants. Then, 31 epitopes restricted by the HLA-A2 molecule were used to generate peptide cocktail vaccines in combination with Poly(I:C), R848 or poly (lactic-co-glycolic acid) nanoparticles, and these vaccines elicited robust and specific CD8+ T cell responses in HLA-A2/DR1 transgenic mice as well as wild-type mice. In contrast to previous research, this study established a modified DC-peptide-PBL cell coculture system using healthy donor PBMCs to validate the in silico predicted epitopes, provided an epitope library restricted by nine of the most prevalent HLA-A allotypes covering broad Asian populations, and identified the HLA-A restrictions of these validated epitopes using competitive peptide binding experiments with HMy2.CIR cell lines expressing the indicated HLA-A allotype, which initially confirmed the in vivo feasibility of 9- or 10-mer peptide cocktail vaccines against SARS-CoV-2. These data will facilitate the design and development of vaccines that induce antiviral CD8+ T cell responses in COVID-19 patients.

Reference

https://www.nature.com/articles/s41423-021-00784-8

Prognostic value of neutrophil-to-lymphocyte ratio in COVID-19 compared with Influenza and respiratory syncytial virus infection

Abstract

A high neutrophil to lymphocyte ratio (NLR) is considered an unfavorable prognostic factor in various diseases, including COVID-19. The prognostic value of NLR in other respiratory viral infections, such as Influenza, has not hitherto been extensively studied. We aimed to compare the prognostic value of NLR in COVID-19, Influenza and Respiratory Syncytial Virus infection (RSV). A retrospective cohort of COVID-19, Influenza and RSV patients admitted to the Tel Aviv Medical Center from January 2010 to October 2020 was analyzed. Laboratory, demographic, and clinical parameters were collected. Two way analyses of variance (ANOVA) was used to compare the association between NLR values and poor outcomes among the three groups. ROC curve analyses for each virus was applied to test the discrimination ability of NLR. 722 COVID-19, 2213 influenza and 482 RSV patients were included. Above the age of 50, NLR at admission was significantly lower among COVID-19 patients ($P < 0.001$). NLR was associated with poor clinical outcome only in the COVID-19 group. ROC curve analysis was performed; the area under curve of poor outcomes for COVID-19 was 0.68, compared with 0.57 and 0.58 for Influenza and RSV respectively. In the COVID-19 group, multivariate logistic regression identified a high NLR (defined as a value above 6.82) to be a prognostic factor for poor clinical outcome, after adjusting for age, sex and Charlson comorbidity score (odds ratio of 2.9, $P < 0.001$). NLR at admission is lower and has more prognostic value in COVID-19 patients, when compared to Influenza and RSV.

Reference

https://www.nature.com/articles/s41598-021-00927-x

BNT162b2 and mRNA-1273 COVID-19 vaccine effectiveness against the SARS-CoV-2 Delta variant in Qatar

Abstract

With the global expansion of the highly transmissible SARS-CoV-2 Delta (B.1.617.2) variant, we conducted a matched test-negative case–control study to assess the real-world effectiveness of COVID-19 messenger RNA vaccines against infection with Delta in Qatar's population. BNT162b2 effectiveness against any, symptomatic or asymptomatic, Delta infection was 45.3% (95% CI, 22.0–61.6%) ≥14 d after the first vaccine dose, but only 51.9% (95% CI, 47.0–56.4%) ≥14 d after the second dose, with 50% of fully vaccinated individuals receiving their second dose before 11 May 2021. Corresponding mRNA-1273 effectiveness ≥14 d after the first or second dose was 73.7% (95% CI, 58.1–83.5%) and 73.1% (95% CI, 67.5–77.8%), respectively. Notably, effectiveness against Delta-induced severe, critical or fatal disease was 93.4% (95% CI, 85.4–97.0%) for BNT162b2 and 96.1% (95% CI, 71.6–99.5%) for mRNA-1273 ≥ 14 d after the second dose. Our findings show robust effectiveness for both BNT162b2 and mRNA-1273 in preventing Delta hospitalization and death in Qatar's population, despite lower effectiveness in preventing infection, particularly for the BNT162b2 vaccine.

Reference

https://www.nature.com/articles/s41591-021-01583-4

An oral SARS-CoV-2 Mpro inhibitor clinical candidate for the treatment of COVID-19

Abstract

The worldwide outbreak of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has become a global pandemic. Alongside vaccines, antiviral therapeutics are an important part of the healthcare response to counter the ongoing threat presented by COVID-19. Here, we report the discovery and characterization of PF-07321332, an orally bioavailable SARS-CoV-2 main protease inhibitor with in vitro pan-human coronavirus antiviral activity and excellent off-target selectivity and in vivo safety profiles. PF-07321332 has demonstrated oral activity in a mouse-adapted SARS-CoV-2 model and has achieved

oral plasma concentrations exceeding the in vitro antiviral cell potency in a phase I clinical trial in healthy human participants.

Reference

https://www.science.org/doi/10.1126/science.abl4784

Exponential growth, high prevalence of SARS-CoV-2, and vaccine effectiveness associated with the Delta variant

Abstract

SARS-CoV-2 infections were rising during early summer 2021 in many countries associated with the Delta variant. We assessed RT-PCR swab-positivity in the REal-time Assessment of Community Transmission-1 (REACT-1) study in England. We observed sustained exponential growth with average doubling time (June-July 2021) of 25 days driven by complete replacement of Alpha variant by Delta, and by high prevalence at younger less-vaccinated ages. Unvaccinated people were three times more likely than double-vaccinated people to test positive. However, after adjusting for age and other variables, vaccine effectiveness for double-vaccinated people was estimated at between ~50% and ~60% during this period in England. Increased social mixing in the presence of Delta had the potential to generate sustained growth in infections, even at high levels of vaccination.

Reference

https://www.science.org/doi/10.1126/science.abl9551

BNT162b2 vaccination induces durable SARS-CoV-2 specific T cells with a stem cell memory phenotype

Abstract

Vaccination against SARS-CoV-2 is effective in preventing hospitalization from severe COVID-19. However, multiple reports of break-through infections and of waning antibody titers have raised concerns on the durability of the vaccine, and current vaccination strategies now propose administration of a third dose. Here, we monitored T cell responses to the Spike protein of SARS-CoV-2 in 71 healthy donors vaccinated with two doses of the Pfizer–BioNTech mRNA vaccine (BNT162b2) for up to 6 months after

vaccination. We found that vaccination induced the development of a sustained anti-viral CD4+ and CD8+ T cell response. These cells appeared before the development of high antibody titers, displayed markers of immunological maturity and stem cell memory, survived the physiological contraction of the immune response and persisted for at least 6 months. Collectively, these data show that vaccination with BNT162b2 elicits an immunologically competent and long-lived SARS-CoV-2-specific T cell population.

Reference

https://www.science.org/doi/10.1126/sciimmunol.abl5344

Publication Date: Nov 01, 2021

Association between prognostic factors and the outcomes of patients infected with SARS-CoV-2 harboring multiple spike protein mutations

Abstract

The outcome of SARS-CoV-2 infection is determined by multiple factors, including the viral, host genetics, age, and comorbidities. This study investigated the association between prognostic factors and disease outcomes of patients infected by SARS-CoV-2 with multiple S protein mutations. Fifty-one COVID-19 patients were recruited in this study. Whole-genome sequencing of 170 full-genomes of SARS-CoV-2 was conducted with the Illumina MiSeq sequencer. Most patients (47%) had mild symptoms of COVID-19 followed by moderate (19.6%), no symptoms (13.7%), severe (4%), and critical (2%). Mortality was found in 13.7% of the COVID-19 patients. There was a significant difference between the age of hospitalized patients (53.4 ± 18 years) and the age of non-hospitalized patients (34.6 ± 19) ($p = 0.001$). The patients' hospitalization was strongly associated with hypertension, diabetes, and anticoagulant and were strongly significant with the OR of 17 (95% CI 2–144; $p = 0.001$), 4.47 (95% CI 1.07–18.58; $p = 0.039$), and 27.97 (95% CI 1.54–507.13; $p = 0.02$), respectively; while the patients' mortality was significantly correlated with patients' age, anticoagulant, steroid, and diabetes, with OR of 8.44 (95% CI 1.5–47.49; $p = 0.016$), 46.8 (95% CI 4.63–472.77; $p = 0.001$), 15.75 (95% CI 2–123.86; $p = 0.009$), and 8.5 (95% CI 1.43–50.66; $p = 0.019$), respectively. This study found the clade: L (2%), GH (84.3%), GR

(11.7%), and O (2%). Besides the D614G mutation, we found L5F (18.8%), V213A (18.8%), and S689R (8.3%). No significant association between multiple S protein mutations and the patients' hospitalization or mortality. Multivariate analysis revealed that hypertension and anticoagulant were the significant factors influencing the hospitalization and mortality of patients with COVID-19 with an OR of 17.06 (95% CI 2.02–144.36; p = 0.009) and 46.8 (95% CI 4.63–472.77; p = 0.001), respectively. Moreover, the multiple S protein mutations almost reached a strong association with patients' hospitalization (p = 0.07). We concluded that hypertension and anticoagulant therapy have a significant impact on COVID-19 outcomes. This study also suggests that multiple S protein mutations may impact the COVID-19 outcomes. This further emphasized the significance of monitoring SARS-CoV-2 variants through genomic surveillance, particularly those that may impact the COVID-19 outcomes.

Reference

https://www.nature.com/articles/s41598-021-00459-4

A live measles-vectored COVID-19 vaccine induces strong immunity and protection from SARS-CoV-2 challenge in mice and hamsters

Abstract

Several COVID-19 vaccines have now been deployed to tackle the SARS-CoV-2 pandemic, most of them based on messenger RNA or adenovirus vectors.The duration of protection afforded by these vaccines is unknown, as well as their capacity to protect from emerging new variants. To provide sufficient coverage for the world population, additional strategies need to be tested. The live pediatric measles vaccine (MV) is an attractive approach, given its extensive safety and efficacy history, along with its established large-scale manufacturing capacity. We develop an MV-based SARS-CoV-2 vaccine expressing the prefusion-stabilized, membrane-anchored full-length S antigen, which proves to be efficient at eliciting strong Th1-dominant T-cell responses and high neutralizing antibody titers. In both mouse and golden Syrian hamster models, these responses protect the animals from intranasal infectious challenge. Additionally, the elicited antibodies efficiently neutralize in vitro the three currently circulating variants of SARS-CoV-2.

Reference

https://www.nature.com/articles/s41467-021-26506-2

Viral loads of Delta-variant SARS-CoV-2 breakthrough infections after vaccination and booster with BNT162b2

Abstract

The effectiveness of the coronavirus disease 2019 (COVID-19) BNT162b2 vaccine in preventing disease and reducing viral loads of breakthrough infections (BTIs) has been decreasing, concomitantly with the rise of the Delta variant of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). However, it is unclear whether the observed decreased effectiveness of the vaccine in reducing viral loads is inherent to the Delta variant or is dependent on time from immunization. By analyzing viral loads of over 16,000 infections during the current, Delta-variant-dominated pandemic wave in Israel, we found that BTIs in recently fully vaccinated individuals have lower viral loads than infections in unvaccinated individuals. However, this effect starts to decline 2 months after vaccination and ultimately vanishes 6 months or longer after vaccination. Notably, we found that the effect of BNT162b2 on reducing BTI viral loads is restored after a booster dose. These results suggest that BNT162b2 might decrease the infectiousness of BTIs even with the Delta variant, and that, although this protective effect declines with time, it can be restored, at least temporarily, with a third, booster, vaccine dose.

Reference

https://www.nature.com/articles/s41591-021-01575-4

A novel wastewater-based epidemiology indexing method predicts SARS-CoV-2 disease prevalence across treatment facilities in metropolitan and regional populations

Abstract

There is a need for wastewater based epidemiological (WBE) methods that integrate multiple, variously sized surveillance sites across geographic areas. We developed a novel indexing method, Melvin’s Index, that provides a normalized and standardized metric of wastewater pathogen load for qPCR assays that is resilient to surveillance site variation. To demonstrate the utility of Melvin’s Index, we used qRT-PCR to measure

SARS-CoV-2 genomic RNA levels in influent wastewater from 19 municipal wastewater treatment facilities (WWTF's) of varying sizes and served populations across the state of Minnesota during the Summer of 2020. SARS-CoV-2 RNA was detected at each WWTF during the 20-week sampling period at a mean concentration of 8.5 × 104 genome copies/L (range 3.2 × 102–1.2 × 109 genome copies/L). Lag analysis of trends in Melvin's Index values and clinical COVID-19 cases showed that increases in indexed wastewater SARS-CoV-2 levels precede new clinical cases by 15–17 days at the statewide level and by up to 25 days at the regional/county level. Melvin's Index is a reliable WBE method and can be applied to both WWTFs that serve a wide range of population sizes and to large regions that are served by multiple WWTFs.

Reference

https://www.nature.com/articles/s41598-021-00853-y

Publication Date: Oct 29, 2021

Multi-omic approach identifies a transcriptional network coupling innate immune response to proliferation in the blood of COVID-19 cancer patients

Abstract

Clinical outcomes of COVID-19 patients are worsened by the presence of co-morbidities, especially cancer leading to elevated mortality rates. SARS-CoV-2 infection is known to alter immune system homeostasis. Whether cancer patients developing COVID-19 present alterations of immune functions which might contribute to worse outcomes have so far been poorly investigated. We conducted a multi-omic analysis of immunological parameters in peripheral blood mononuclear cells (PBMCs) of COVID-19 patients with and without cancer. Healthy donors and SARS-CoV-2-negative cancer patients were also included as controls. At the infection peak, cytokine multiplex analysis of blood samples, cytometry by time of flight (CyTOF) cell population analyses, and Nanostring gene expression using Pancancer array on PBMCs were performed. We found that eight pro-inflammatory factors (IL-6, IL-8, IL-13, IL-1ra, MIP-1a, IP-10) out of 27 analyzed serum cytokines were modulated in COVID-19 patients irrespective of cancer status. Diverse subpopulations of T lymphocytes such as CD8+T, CD4+T central memory, Mucosal-associated invariant T (MAIT), natural killer (NK), and γδ T

cells were reduced, while B plasmablasts were expanded in COVID-19 cancer patients. Our findings illustrate a repertoire of aberrant alterations of gene expression in circulating immune cells of COVID-19 cancer patients. A 19-gene expression signature of PBMCs is able to discriminate COVID-19 patients with and without solid cancers. Gene set enrichment analysis highlights an increased gene expression linked to Interferon α, γ, α/β response and signaling which paired with aberrant cell cycle regulation in cancer patients. Ten out of the 19 genes, validated in a real-world consecutive cohort, were specific of COVID-19 cancer patients independently from different cancer types and stages of the diseases, and useful to stratify patients in a COVID-19 disease severity-manner. We also unveil a transcriptional network involving gene regulators of both inflammation response and proliferation in PBMCs of COVID-19 cancer patients.

Reference

https://www.nature.com/articles/s41419-021-04299-y

Clinical practices underlie COVID-19 patient respiratory microbiome composition and its interactions with the host

Abstract

Understanding the pathology of COVID-19 is a global research priority. Early evidence suggests that the respiratory microbiome may be playing a role in disease progression, yet current studies report contradictory results. Here, we examine potential confounders in COVID-19 respiratory microbiome studies by analyzing the upper (n = 58) and lower (n = 35) respiratory tract microbiome in well-phenotyped COVID-19 patients and controls combining microbiome sequencing, viral load determination, and immunoprofiling. We find that time in the intensive care unit and type of oxygen support, as well as associated treatments such as antibiotic usage, explain the most variation within the upper respiratory tract microbiome, while SARS-CoV-2 viral load has a reduced impact. Specifically, mechanical ventilation is linked to altered community structure and significant shifts in oral taxa previously associated with COVID-19. Single-cell transcriptomics of the lower respiratory tract of COVID-19 patients identifies specific oral bacteria in physical association with proinflammatory immune cells, which show higher levels of inflammatory markers. Overall, our findings suggest confounders are

driving contradictory results in current COVID-19 microbiome studies and careful attention needs to be paid to ICU stay and type of oxygen support, as bacteria favored in these conditions may contribute to the inflammatory phenotypes observed in severe COVID-19 patients.

Reference

https://www.nature.com/articles/s41467-021-26500-8

Direct SARS-CoV-2 infection of the human inner ear may underlie COVID-19-associated audiovestibular dysfunction

Abstract

Background: COVID-19 is a pandemic respiratory and vascular disease caused by SARS-CoV-2 virus. There is a growing number of sensory deficits associated with COVID-19 and molecular mechanisms underlying these deficits are incompletely understood.

Methods: We report a series of ten COVID-19 patients with audiovestibular symptoms such as hearing loss, vestibular dysfunction and tinnitus. To investigate the causal relationship between SARS-CoV-2 and audiovestibular dysfunction, we examine human inner ear tissue, human inner ear in vitro cellular models, and mouse inner ear tissue.

Results: We demonstrate that adult human inner ear tissue co-expresses the angiotensin-converting enzyme 2 (ACE2) receptor for SARS-CoV-2 virus, and the transmembrane protease serine 2 (TMPRSS2) and FURIN cofactors required for virus entry. Furthermore, hair cells and Schwann cells in explanted human vestibular tissue can be infected by SARS-CoV-2, as demonstrated by confocal microscopy. We establish three human induced pluripotent stem cell (hiPSC)-derived in vitro models of the inner ear for infection: two-dimensional otic prosensory cells (OPCs) and Schwann cell precursors (SCPs), and three-dimensional inner ear organoids. Both OPCs and SCPs express ACE2, TMPRSS2, and FURIN, with lower ACE2 and FURIN expression in SCPs. OPCs are permissive to SARS-CoV-2 infection; lower infection rates exist in isogenic SCPs. The inner ear organoids show that hair cells express ACE2 and are targets for SARS-CoV-2.

Conclusions: Our results provide mechanistic explanations of audiovestibular dysfunction in COVID-19 patients and introduce hiPSC-derived systems for studying infectious human otologic disease.

Reference

https://www.nature.com/articles/s43856-021-00044-w

The evaluation of novel oral vaccines based on self-amplifying RNA lipid nanparticles (saRNA LNPs), saRNA transfected *Lactobacillus plantarum* LNPs, and saRNA transfected Lactobacillus plantarum to neutralize SARS-CoV-2 variants alpha and delta

Abstract

The aim of this study was to present and evaluate novel oral vaccines, based on self-amplifying RNA lipid nanparticles (saRNA LNPs), saRNA transfected Lactobacillus plantarum LNPs, and saRNA transfected *Lactobacillus plantaru*m, to neutralize severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) variants alpha and delta. After invitro evaluation of the oral vaccines on HEK293T/17 cells, we found that saRNA LNPs, saRNA transfected *Lactobacillus plantarum* LNPs, and saRNA transfected *Lactobacillus plantarum* could express S-protein at both mRNA and protein levels. In the next step, BALB/c mice were orally vaccinated with saRNA LNPs, saRNA transfected *Lactobacillus plantarum* LNPs, and saRNA transfected Lactobacillus plantarum at weeks 1 and 3. Importantly, a high titer of IgG and IgA was observed by all of them, sharply in week 6 ($P < 0.05$). In all study groups, their ratio of IgG2a/IgG1 was upper 1, indicating Th1-biased responses. Wild-type viral neutralization assay showed that the secreted antibodies in vaccinated mice and recovered COVID-19 patients could neutralize SARS-COV-2 variants alpha and delta. After oral administration of oral vaccines, biodistribution assay was done. It was found that all of them had the same biodistribution pattern. The highest concentration of S-protein was seen in the small intestine, followed by the large intestine and liver.

Reference

https://www.nature.com/articles/s41598-021-00830-5

Anti-spike antibody response to natural SARS-CoV-2 infection in the general population

Abstract

Understanding the trajectory, duration, and determinants of antibody responses after SARS-CoV-2 infection can inform subsequent protection and risk of reinfection, however large-scale representative studies are limited. Here we estimated antibody response after SARS-CoV-2 infection in the general population using representative data from 7,256 United Kingdom COVID-19 infection survey participants who had positive swab SARS-CoV-2 PCR tests from 26-April-2020 to 14-June-2021. A latent class model classified 24% of participants as 'non-responders' not developing anti-spike antibodies, who were older, had higher SARS-CoV-2 cycle threshold values during infection (i.e. lower viral burden), and less frequently reported any symptoms. Among those who seroconverted, using Bayesian linear mixed models, the estimated anti-spike IgG peak level was 7.3-fold higher than the level previously associated with 50% protection against reinfection, with higher peak levels in older participants and those of non-white ethnicity. The estimated anti-spike IgG half-life was 184 days, being longer in females and those of white ethnicity. We estimated antibody levels associated with protection against reinfection likely last 1.5-2 years on average, with levels associated with protection from severe infection present for several years. These estimates could inform planning for vaccination booster strategies.

Reference

https://www.nature.com/articles/s41467-021-26479-2

Low-dose *in vivo* protection and neutralization across SARS-CoV-2 variants by monoclonal antibody combinations

Abstract

Prevention of viral escape and increased coverage against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants of concern require therapeutic monoclonal antibodies (mAbs) targeting multiple sites of vulnerability on the coronavirus spike glycoprotein. Here we identify several potent neutralizing antibodies directed against either the N-terminal domain (NTD) or the receptor-binding domain (RBD) of the

spike protein. Administered in combinations, these mAbs provided low-dose protection against SARS-CoV-2 infection in the K18-human angiotensin-converting enzyme 2 mouse model, using both neutralization and Fc effector antibody functions. The RBD mAb WRAIR-2125, which targets residue F486 through a unique heavy-chain and light-chain pairing, demonstrated potent neutralizing activity against all major SARS-CoV-2 variants of concern. In combination with NTD and other RBD mAbs, WRAIR-2125 also prevented viral escape. These data demonstrate that NTD/RBD mAb combinations confer potent protection, likely leveraging complementary mechanisms of viral inactivation and clearance.

Reference

https://www.nature.com/articles/s41590-021-01068-z

Community transmission and viral load kinetics of the SARS-CoV-2 delta (B.1.617.2) variant in vaccinated and unvaccinated individuals in the UK: A prospective, longitudinal, cohort study

Abstract

Background: The SARS-CoV-2 delta (B.1.617.2) variant is highly transmissible and spreading globally, including in populations with high vaccination rates. We aimed to investigate transmission and viral load kinetics in vaccinated and unvaccinated individuals with mild delta variant infection in the community.

Methods: Between Sept 13, 2020, and Sept 15, 2021, 602 community contacts (identified via the UK contract-tracing system) of 471 UK COVID-19 index cases were recruited to the Assessment of Transmission and Contagiousness of COVID-19 in Contacts cohort study and contributed 8145 upper respiratory tract samples from daily sampling for up to 20 days. Household and non-household exposed contacts aged 5 years or older were eligible for recruitment if they could provide informed consent and agree to self-swabbing of the upper respiratory tract. We analysed transmission risk by vaccination status for 231 contacts exposed to 162 epidemiologically linked delta variant-infected index cases. We compared viral load trajectories from fully vaccinated individuals with delta infection (n=29) with unvaccinated individuals with delta (n=16), alpha (B.1.1.7; n=39), and pre-alpha (n=49) infections. Primary outcomes for the epidemiological analysis were to assess the secondary attack rate (SAR) in household

contacts stratified by contact vaccination status and the index cases' vaccination status. Primary outcomes for the viral load kinetics analysis were to detect differences in the peak viral load, viral growth rate, and viral decline rate between participants according to SARS-CoV-2 variant and vaccination status.

Findings: The SAR in household contacts exposed to the delta variant was 25% (95% CI 18–33) for fully vaccinated individuals compared with 38% (24–53) in unvaccinated individuals. The median time between second vaccine dose and study recruitment in fully vaccinated contacts was longer for infected individuals (median 101 days [IQR 74–120]) than for uninfected individuals (64 days [32–97], p=0·001). SAR among household contacts exposed to fully vaccinated index cases was similar to household contacts exposed to unvaccinated index cases (25% [95% CI 15–35] for vaccinated vs 23% [15–31] for unvaccinated). 12 (39%) of 31 infections in fully vaccinated household contacts arose from fully vaccinated epidemiologically linked index cases, further confirmed by genomic and virological analysis in three index case–contact pairs. Although peak viral load did not differ by vaccination status or variant type, it increased modestly with age (difference of 0·39 [95% credible interval –0·03 to 0·79] in peak log10 viral load per mL between those aged 10 years and 50 years). Fully vaccinated individuals with delta variant infection had a faster (posterior probability >0·84) mean rate of viral load decline (0·95 log10 copies per mL per day) than did unvaccinated individuals with pre-alpha (0·69), alpha (0·82), or delta (0·79) variant infections. Within individuals, faster viral load growth was correlated with higher peak viral load (correlation 0·42 [95% credible interval 0·13 to 0·65]) and slower decline (–0·44 [–0·67 to –0·18]).

Interpretation: Vaccination reduces the risk of delta variant infection and accelerates viral clearance. Nonetheless, fully vaccinated individuals with breakthrough infections have peak viral load similar to unvaccinated cases and can efficiently transmit infection in household settings, including to fully vaccinated contacts. Host–virus interactions early in infection may shape the entire viral trajectory.

Reference

https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00648-4/fulltext

Effect of anti-interleukin drugs in patients with COVID-19 and signs of cytokine release syndrome (COV-AID): A factorial, randomised, controlled trial

Abstract

Background: Infections with SARS-CoV-2 continue to cause significant morbidity and mortality. Interleukin (IL)-1 and IL-6 blockade have been proposed as therapeutic strategies in COVID-19, but study outcomes have been conflicting. We sought to study whether blockade of the IL-6 or IL-1 pathway shortened the time to clinical improvement in patients with COVID-19, hypoxic respiratory failure, and signs of systemic cytokine release syndrome.

Methods: We did a prospective, multicentre, open-label, randomised, controlled trial, in hospitalised patients with COVID-19, hypoxia, and signs of a cytokine release syndrome across 16 hospitals in Belgium. Eligible patients had a proven diagnosis of COVID-19 with symptoms between 6 and 16 days, a ratio of the partial pressure of oxygen to the fraction of inspired oxygen (PaO2:FiO2) of less than 350 mm Hg on room air or less than 280 mm Hg on supplemental oxygen, and signs of a cytokine release syndrome in their serum (either a single ferritin measurement of more than 2000 µg/L and immediately requiring high flow oxygen or mechanical ventilation, or a ferritin concentration of more than 1000 µg/L, which had been increasing over the previous 24 h, or lymphopenia below 800/mL with two of the following criteria: an increasing ferritin concentration of more than 700 µg/L, an increasing lactate dehydrogenase concentration of more than 300 international units per L, an increasing C-reactive protein concentration of more than 70 mg/L, or an increasing D-dimers concentration of more than 1000 ng/mL). The COV-AID trial has a 2 × 2 factorial design to evaluate IL-1 blockade versus no IL-1 blockade and IL-6 blockade versus no IL-6 blockade. Patients were randomly assigned by means of permuted block randomisation with varying block size and stratification by centre. In a first randomisation, patients were assigned to receive subcutaneous anakinra once daily (100 mg) for 28 days or until discharge, or to receive no IL-1 blockade (1:2). In a second randomisation step, patients were allocated to receive a single dose of siltuximab (11 mg/kg) intravenously, or a single dose of tocilizumab (8 mg/kg) intravenously, or to receive no IL-6 blockade (1:1:1). The primary outcome was the time to clinical improvement, defined as time from randomisation to an increase of at least two points on a 6-category ordinal scale or to discharge from

hospital alive. The primary and supportive efficacy endpoints were assessed in the intention-to-treat population. Safety was assessed in the safety population. This study is registered online with ClinicalTrials.gov (NCT04330638) and EudraCT (2020-001500-41) and is complete.

Findings: Between April 4, and Dec 6, 2020, 342 patients were randomly assigned to IL-1 blockade (n=112) or no IL-1 blockade (n=230) and simultaneously randomly assigned to IL-6 blockade (n=227; 114 for tocilizumab and 113 for siltuximab) or no IL-6 blockade (n=115). Most patients were male (265 [77%] of 342), median age was 65 years (IQR 54–73), and median Systematic Organ Failure Assessment (SOFA) score at randomisation was 3 (2–4). All 342 patients were included in the primary intention-to-treat analysis. The estimated median time to clinical improvement was 12 days (95% CI 10–16) in the IL-1 blockade group versus 12 days (10–15) in the no IL-1 blockade group (hazard ratio [HR] 0·94 [95% CI 0·73–1·21]). For the IL-6 blockade group, the estimated median time to clinical improvement was 11 days (95% CI 10–16) versus 12 days (11–16) in the no IL-6 blockade group (HR 1·00 [0·78–1·29]). 55 patients died during the study, but no evidence for differences in mortality between treatment groups was found. The incidence of serious adverse events and serious infections was similar across study groups.

Interpretation: Drugs targeting IL-1 or IL-6 did not shorten the time to clinical improvement in this sample of patients with COVID-19, hypoxic respiratory failure, low SOFA score, and low baseline mortality risk.

Reference

https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00377-5/fulltext

Complete protection by a single-dose skin patch–delivered SARS-CoV-2 spike vaccine

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has infected more than 160 million people and resulted in more than 3.3 million deaths, and despite the availability of multiple vaccines, the world still faces many challenges with their rollout. Here, we use the high-density microarray patch (HD-MAP) to deliver a SARS-CoV-2 spike subunit vaccine directly to the skin. We show that the vaccine is thermostable on the patches, with patch delivery enhancing both cellular and antibody immune

responses. Elicited antibodies potently neutralize clinically relevant isolates including the Alpha and Beta variants. Last, a single dose of HD-MAP–delivered spike provided complete protection from a lethal virus challenge in an ACE2-transgenic mouse model. Collectively, these data show that HD-MAP delivery of a SARS-CoV-2 vaccine was superior to traditional needle-and-syringe vaccination and may be a significant addition to the ongoing COVID-19 (coronavirus disease 2019) pandemic.

Reference

https://www.science.org/doi/10.1126/sciadv.abj8065

Publication Date: Oct 28, 2021

Quantification of airborne SARS-CoV-2 genomic particles in different hospital settings

Abstract

We quantified the presence of SARS-CoV-2 RNA in the air of different hospital settings and the autopsy room of the largest medical centre in Sao Paulo, Brazil. Real-time reverse-transcription PCR was used to determine the presence of the envelope protein of SARS-CoV-2 and the nucleocapsid protein genes. The E-gene was detected in 5 out of 6 samples at the ICU-COVID-19 ward and in 5 out of 7 samples at the ward-COVID-19. Similarly, in the non-dedicated facilities, the E-gene was detected in 5 out of 6 samples collected in the ICU and 4 out of 7 samples in the ward. In the necropsy room, 6 out of 7 samples were positive for the E-gene. When both wards were compared, the non-COVID ward presented a significantly higher concentration of the E-gene than in the COVID-19 ward ($p = 0.003$). There was no significant difference in E-gene concentration between the ICU-COVID-19 and the ICU ($p = 0.548$). Likewise, there was no significant difference among E-gene concentrations found in the autopsy room versus the ICUs and wards (dedicated or not) ($p = 0.245$). Our results show the widespread presence of aerosol contamination in different hospital units.

Reference

https://www.nature.com/articles/s41374-021-00663-w

Differential dynamics of peripheral immune responses to acute SARS-CoV-2 infection in older adults

Abstract

In this study, peripheral blood mononuclear cells from young and old patients with COVID-19 were examined phenotypically, transcriptionally and functionally to reveal age-, time- and severity-specific adaptations. Gene signatures within memory B cells and plasmablasts correlated with reduced frequency of antigen-specific B cells and neutralizing antibodies in older patients with severe COVID-19. Moreover, these patients exhibited exacerbated T cell lymphopenia, which correlated with lower plasma interleukin-2, and diminished antigen-specific T cell responses. Single-cell RNA sequencing revealed augmented signatures of activation, exhaustion, cytotoxicity and type I interferon signaling in memory T and natural killer cells with age. Although cytokine storm was evident in both age groups, older individuals exhibited elevated levels of myeloid cell recruiting factors. Furthermore, we observed redistribution of monocyte and dendritic cell subsets and emergence of a suppressive phenotype with severe disease, which was reversed only in young patients over time. This analysis provides new insights into the impact of aging on COVID-19.

Reference

https://www.nature.com/articles/s43587-021-00127-2

Effectiveness of ChAdOx1 vaccine in older adults during SARS-CoV-2 Gamma variant circulation in São Paulo

Abstract

A two-dose regimen of the Oxford-AstraZeneca (ChAdOx1) Covid-19 vaccine with an inter-dose interval of three months has been implemented in many countries with restricted vaccine supply. However, there is limited evidence for the effectiveness of ChAdOx1 by dose in elderly populations in countries with high prevalence of the Gamma variant of SARS-CoV-2. Here, we estimate ChAdOx1 effectiveness by dose against the primary endpoint of RT-PCR-confirmed Covid-19, and secondary endpoints of Covid-19 hospitalization and Covid-19-related death, in adults aged ≥60 years during an epidemic with high Gamma variant prevalence in São Paulo state, Brazil using a

matched, test-negative case-control study. Starting 28 days after the first dose, effectiveness of a single dose of ChAdOx1 is 33.4% (95% CI, 26.4–39.7) against Covid-19, 55.1% (95% CI, 46.6–62.2) against hospitalization, and 61.8% (95% CI, 48.9–71.4) against death. Starting 14 days after the second dose, effectiveness of the two-dose schedule is 77.9% (95% CI, 69.2–84.2) against Covid-19, 87.6% (95% CI, 78.2–92.9) against hospitalization, and 93.6% (95% CI, 81.9–97.7) against death. Completion of the ChAdOx1 vaccine schedule affords significantly increased protection over a single dose against mild and severe Covid-19 outcomes in elderly individuals during widespread Gamma variant circulation.

Reference

https://www.nature.com/articles/s41467-021-26459-6

Co-infection of SARS-CoV-2 and influenza virus causes more severe and prolonged pneumonia in hamsters

Abstract

Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is currently a serious public health concern worldwide. Notably, co-infection with other pathogens may worsen the severity of COVID-19 symptoms and increase fatality. Here, we show that co-infection with influenza A virus (IAV) causes more severe body weight loss and more severe and prolonged pneumonia in SARS-CoV-2-infected hamsters. Each virus can efficiently spread in the lungs without interference by the other. However, in immunohistochemical analyses, SARS-CoV-2 and IAV were not detected at the same sites in the respiratory organs of co-infected hamsters, suggesting that either the two viruses may have different cell tropisms in vivo or each virus may inhibit the infection and/or growth of the other within a cell or adjacent areas in the organs. Furthermore, a significant increase in IL-6 was detected in the sera of hamsters co-infected with SARS-CoV-2 and IAV at 7 and 10 days post-infection, suggesting that IL-6 may be involved in the increased severity of pneumonia. Our results strongly suggest that IAV co-infection with SARS-CoV-2 can have serious health risks and increased caution should be applied in such cases.

Reference

https://www.nature.com/articles/s41598-021-00809-2

A SARS-CoV-2 spike ferritin nanoparticle vaccine protects hamsters against Alpha and Beta virus variant challenge

Abstract

The emergence of SARS-CoV-2 variants of concern (VOC) requires adequate coverage of vaccine protection. We evaluated whether a SARS-CoV-2 spike ferritin nanoparticle vaccine (SpFN), adjuvanted with the Army Liposomal Formulation QS21 (ALFQ), conferred protection against the Alpha (B.1.1.7), and Beta (B.1.351) VOCs in Syrian golden hamsters. SpFN-ALFQ was administered as either single or double-vaccination (0 and 4 week) regimens, using a high (10 μg) or low (0.2 μg) dose. Animals were intranasally challenged at week 11. Binding antibody responses were comparable between high- and low-dose groups. Neutralizing antibody titers were equivalent against WA1, B.1.1.7, and B.1.351 variants following two high dose vaccinations. Dose-dependent SpFN-ALFQ vaccination protected against SARS-CoV-2-induced disease and viral replication following intranasal B.1.1.7 or B.1.351 challenge, as evidenced by reduced weight loss, lung pathology, and lung and nasal turbinate viral burden. These data support the development of SpFN-ALFQ as a broadly protective, next-generation SARS-CoV-2 vaccine.

Reference

https://www.nature.com/articles/s41541-021-00392-7