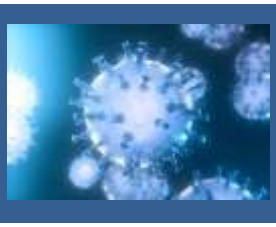
COVID-19

Nov 04 – 10, 2021



RESEARCH PUBLICATIONS

Publication Date: Nov 10, 2021

Enhanced protective immunity against SARS-CoV-2 elicited by a VSV vector expressing a chimeric spike protein

Abstract

SARS-CoV-2 and SARS-CoV are genetically related coronavirus and share the same cellular receptor ACE2. By replacing the VSV glycoprotein with the spikes (S) of SARS-CoV-2 and SARS-CoV, we generated two replication-competent recombinant viruses, rVSV-SARS-CoV-2 and rVSV-SARS-CoV. Using wild-type and human ACE2 (hACE2) knock-in mouse models, we found a single dose of rVSV-SARS-CoV could elicit strong humoral immune response via both intranasal (i.n.) and intramuscular (i.m.) routes. Despite the high genetic similarity between SARS-CoV-2 and SARS-CoV, no obvious cross-neutralizing activity was observed in the immunized mice sera. In macaques, neutralizing antibody (NAb) titers induced by one i.n. dose of rVSV-SARS-CoV-2 were eight-fold higher than those by a single i.m. dose. Thus, our data indicates that rVSV-SARS-CoV-2 might be suitable for i.n. administration instead of the traditional i.m. immunization in human. Because rVSV-SARS-CoV elicited significantly stronger NAb responses than rVSV-SARS-CoV-2 in a route-independent manner, we generated a chimeric antigen by replacing the receptor binding domain (RBD) of SARS-CoV S with that from the SARS-CoV-2. rVSV expressing the chimera (rVSV-SARS-CoV/2-RBD) induced significantly increased NAbs against SARS-CoV-2 in mice and macaques than rVSV-SARS-CoV-2, with a safe Th1-biased response. Serum immunized with rVSV-SARS-CoV/2-RBD showed no cross-reactivity with SARS-CoV. hACE2 mice receiving a single i.m. dose of either rVSV-SARS-CoV-2 or rVSV-SARS-CoV/2-RBD were fully protected against SARS-CoV-2 challenge without obvious lesions in the lungs. Our

results suggest that transplantation of SARS-CoV-2 RBD into the S protein of SARS-CoV might be a promising antigen design for COVID-19 vaccines.

Reference

https://www.nature.com/articles/s41392-021-00797-9

Infection control in the intensive care unit: expert consensus statements for SARS-CoV-2 using a Delphi method

Abstract

During the current COVID-19 pandemic, health-care workers and uninfected patients in intensive care units (ICUs) are at risk of being infected with SARS-CoV-2 as a result of transmission from infected patients and health-care workers. In the absence of high-quality evidence on the transmission of SARS-CoV-2, clinical practice of infection control and prevention in ICUs varies widely. Using a Delphi process, international experts in intensive care, infectious diseases, and infection control developed consensus statements on infection control for SARS-CoV-2 in an ICU. Consensus was achieved for 31 (94%) of 33 statements, from which 25 clinical practice statements were issued. These statements include guidance on ICU design and engineering, health-care worker safety, visiting policy, personal protective equipment, patients and procedures, disinfection, and sterilisation. Consensus was not reached on optimal return to work criteria for health-care workers who were infected with SARS-CoV-2 or the acceptable disinfection strategy for heat-sensitive instruments used for airway management of patients with SARS-CoV-2 infection. Well designed studies are needed to assess the effects of these practice statements and address the remaining uncertainties.

Reference

https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00626-5/fulltext

Clinical outcomes of hypertensive patients with COVID-19 receiving calcium channel blockers: A systematic review and meta-analysis

Abstract

It was aimed to perform a systematic review and meta-analysis to determine the overall effect of the preadmission/prediagnosis use of calcium channel blockers (CCBs) on the clinical outcomes in hypertensive patients with COVID-19. A systematic literature search with no language restriction was conducted in electronic databases in July 2021 to identify eligible studies. A random-effects model was used to estimate the pooled summary measure for outcomes of interest with the preadmission/prediagnosis use of CCBs relative to the nonuse of CCBs at 95% confidence intervals (CIs). The meta-analysis revealed a significant reduction in the odds of all-cause mortality with the preadmission/prediagnosis use of CCBs relative to the nonuse of CCBs (pooled OR = 0.65; 95% CI 0.49–0.86) and a significant reduction in the odds of severe illness with preadmission/prediagnosis use of CCBs relative to the nonuse of CCBs (pooled OR = 0.61; 95% CI 0.44–0.84), and is associated with adequate evidence to reject the model hypothesis of 'no significant difference' at the current sample size. The potential protective effects offered by CCBs in hypertensive patients with COVID-19 merit large-scale prospective investigations.

Reference

https://www.nature.com/articles/s41440-021-00786-z

Humoral and cellular immunogenicity to a second dose of COVID-19 vaccine BNT162b2 in people receiving methotrexate or targeted immunosuppression: A longitudinal cohort study

Abstract

Background: COVID-19 vaccines have robust immunogenicity in the general population. However, data for individuals with immune-mediated inflammatory diseases who are taking immunosuppressants remains scarce. Our previously published cohort study showed that methotrexate, but not targeted biologics, impaired functional humoral immunity to a single dose of COVID-19 vaccine BNT162b2 (Pfizer-BioNTech), whereas

cellular responses were similar. Here, we aimed to assess immune responses following the second dose.

Methods: In this longitudinal cohort study, we recruited individuals with psoriasis who were receiving methotrexate or targeted biological monotherapy (ie, tumour necrosis factor [TNF] inhibitors, interleukin [IL]-17 inhibitors, or IL-23 inhibitors) from a specialist psoriasis centre serving London and South-East England. The healthy control cohort were volunteers without psoriasis, not receiving immunosuppression. Immunogenicity was evaluated immediately before, on day 28 after the first BNT162b2 vaccination and on day 14 after the second dose (administered according to an extended interval regimen). Here, we report immune responses following the second dose. The primary outcomes were humoral immunity to the SARS-CoV-2 spike glycoprotein, defined as titres of total spike-specific IgG and of neutralising antibody to wild-type, alpha (B.1.1.7), and delta (B.1.617.2) SARS-CoV-2 variants, and cellular immunity defined as spike-specific T-cell responses (including numbers of cells producing interferon-γ, IL-2, IL-21).

Findings: Between Jan 14 and April 4, 2021, 121 individuals were recruited, and data were available for 82 participants after the second vaccination. The study population included patients with psoriasis receiving methotrexate (n=14), TNF inhibitors (n=19), IL-17 inhibitors (n=14), IL-23 inhibitors (n=20), and 15 healthy controls, who had received both vaccine doses. The median age of the study population was 44 years (IQR 33–52), with 43 (52%) males and 71 (87%) participants of White ethnicity. All participants had detectable spike-specific antibodies following the second dose, and all groups (methotrexate, targeted biologics, and healthy controls) demonstrated similar neutralising antibody titres against wild-type, alpha, and delta variants. By contrast, a lower proportion of participants on methotrexate (eight [62%] of 13, 95% CI 32–86) and targeted biologics (37 [74%] of 50, 60–85; p=0·38) had detectable T-cell responses following the second vaccine dose, compared with controls (14 [100%] of 14, 77–100; p=0·022). There was no difference in the magnitude of T-cell responses between patients receiving methotrexate (median cytokine-secreting cells per 106 cells 160 [IQR 10–625]), targeted biologics (169 [25–503], p=0·56), and controls (185 [133–328], p=0·41).

Interpretation: Functional humoral immunity (ie, neutralising antibody responses) at 14 days following a second dose of BNT162b2 was not impaired by methotrexate or

targeted biologics. A proportion of patients on immunosuppression did not have detectable T-cell responses following the second dose. The longevity of vaccine-elicited antibody responses is unknown in this population.

Reference

https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(21)00333-7/fulltext

mRNA-1273 COVID-19 vaccination in patients receiving chemotherapy, immunotherapy, or chemoimmunotherapy for solid tumours: A prospective, multicentre, non-inferiority trial

Abstract

Background: Patients with cancer have an increased risk of complications from SARS-CoV-2 infection. Vaccination to prevent COVID-19 is recommended, but data on the immunogenicity and safety of COVID-19 vaccines for patients with solid tumours receiving systemic cancer treatment are scarce. Therefore, we aimed to assess the impact of immunotherapy, chemotherapy, and chemoimmunotherapy on the immunogenicity and safety of the mRNA-1273 (Moderna Biotech, Madrid, Spain) COVID-19 vaccine as part of the Vaccination Against COVID in Cancer (VOICE) trial.

Methods: This prospective, multicentre, non-inferiority trial was done across three centres in the Netherlands. Individuals aged 18 years or older with a life expectancy of more than 12 months were enrolled into four cohorts: individuals without cancer (cohort A [control cohort]), and patients with solid tumours, regardless of stage and histology, treated with immunotherapy (cohort B), chemotherapy (cohort C), or chemoimmunotherapy (cohort D). Participants received two mRNA-1273 vaccinations of 100 μg in 0·5 mL intramuscularly, 28 days apart. The primary endpoint, analysed per protocol (excluding patients with a positive baseline sample [>10 binding antibody units (BAU)/mL], indicating previous SARS-CoV-2 infection), was defined as the SARS-CoV-2 spike S1-specific IgG serum antibody response (ie, SARS-CoV-2-binding antibody concentration of >10 BAU/mL) 28 days after the second vaccination. For the primary endpoint analysis, a non-inferiority design with a margin of 10% was used. We also assessed adverse events in all patients who received at least one vaccination, and recorded solicited adverse events in participants who received at least one vaccination

but excluding those who already had seroconversion (>10 BAU/mL) at baseline. This study is ongoing and is registered with ClinicalTrials.gov, NCT04715438.

Findings: Between Feb 17 and March 12, 2021, 791 participants were enrolled and followed up for a median of 122 days (IQR 118 to 128). A SARS-CoV-2-binding antibody response was found in 240 (100%; 95% CI 98 to 100) of 240 evaluable participants in cohort A, 130 (99%; 96 to >99) of 131 evaluable patients in cohort B, 223 (97%; 94 to 99) of 229 evaluable patients in cohort C, and 143 (100%; 97 to 100) of 143 evaluable patients in cohort D. The SARS-CoV-2-binding antibody response in each patient cohort was non-inferior compared with cohort A. No new safety signals were observed. Grade 3 or worse serious adverse events occurred in no participants in cohort A, three (2%) of 137 patients in cohort B, six (2%) of 244 patients in cohort C, and one (1%) of 163 patients in cohort D, with four events (two of fever, and one each of diarrhoea and febrile neutropenia) potentially related to the vaccination. There were no vaccine-related deaths.

Interpretation: Most patients with cancer develop, while receiving chemotherapy, immunotherapy, or both for a solid tumour, an adequate antibody response to vaccination with the mRNA-1273 COVID-19 vaccine. The vaccine is also safe in these patients. The minority of patients with an inadequate response after two vaccinations might benefit from a third vaccination.

Reference

https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(21)00574-X/fulltext

T-cell and antibody responses to first BNT162b2 vaccine dose in previously infected and SARS-CoV-2-naive UK health-care workers: A multicentre prospective cohort study

Abstract

Background: Previous infection with SARS-CoV-2 affects the immune response to the first dose of the SARS-CoV-2 vaccine. We aimed to compare SARS-CoV-2-specific T-cell and antibody responses in health-care workers with and without previous SARS-CoV-2 infection following a single dose of the BNT162b2 (tozinameran; Pfizer–BioNTech) mRNA vaccine.

Methods: Health-care workers enrolled in the PITCH study were sampled across four hospital sites in the UK (Oxford, Liverpool, Newcastle, and Sheffield). All health-care workers aged 18 years or older consenting to participate in this prospective cohort study were included, with no exclusion criteria applied. Blood samples were collected where possible before vaccination and 28 (±7) days following one or two doses (given 3–4 weeks apart) of the BNT162b2 vaccine. Previous infection was determined by a documented SARS-CoV-2-positive RT-PCR result or the presence of positive anti-SARS-CoV-2 nucleocapsid antibodies. We measured spike-specific IgG antibodies and quantified T-cell responses by interferon-γ enzyme-linked immunospot assay in all participants where samples were available at the time of analysis, comparing SARS-CoV-2-naive individuals to those with previous infection.

Findings: Between Dec 9, 2020, and Feb 9, 2021, 119 SARS-CoV-2-naive and 145 previously infected health-care workers received one dose, and 25 SARS-CoV-2-naive health-care workers received two doses, of the BNT162b2 vaccine. In previously infected health-care workers, the median time from previous infection to vaccination was 268 days (IQR 232–285). At 28 days (IQR 27–33) after a single dose, the spike-specific T-cell response measured in fresh peripheral blood mononuclear cells (PBMCs) was higher in previously infected (n=76) than in infection-naive (n=45) health-care workers (median 284 [IQR 150–461] vs 55 [IQR 24–132] spot-forming units [SFUs] per 106 PBMCs; p<0·0001). With cryopreserved PBMCs, the T-cell response in previously infected individuals (n=52) after one vaccine dose was equivalent to that of infection-naive individuals (n=19) after receiving two vaccine doses (median 152 [IQR 119–275] vs 162 [104–258] SFUs/106 PBMCs; p=1·00). Anti-spike IgG antibody responses following a single dose in 142 previously infected health-care workers (median 270 373 [IQR 203 461–535 188] antibody units [AU] per mL) were higher than in 111 infection-naive health-care workers following one dose (35 001 [17 099–55 341] AU/mL; p<0·0001) and higher than in 25 infection-naive individuals given two doses (180 904 [108 221–242 467] AU/mL; p<0·0001).

Interpretation: A single dose of the BNT162b2 vaccine is likely to provide greater protection against SARS-CoV-2 infection in individuals with previous SARS-CoV-2 infection, than in SARS-CoV-2-naive individuals, including against variants of concern. Future studies should determine the additional benefit of a second dose on the

magnitude and durability of immune responses in individuals vaccinated following infection, alongside evaluation of the impact of extending the interval between vaccine doses.

Reference

https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247(21)00275-5/fulltext

Molecular basis of immune evasion by the Delta and Kappa SARS-CoV-2 variants

Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission leads to the emergence of variants, including the B.1.617.2 (Delta) variant of concern which is causing a new wave of infections and has become globally dominant. We show that these variants dampen the in vitro potency of vaccine-elicited serum neutralizing antibodies and provide a structural framework for describing their immune evasion. Mutations in the B.1.617.1 (Kappa) and B.1.617.2 (Delta) spike glycoproteins abrogate recognition by several monoclonal antibodies via alteration of key antigenic sites, including remodeling of the B.1.617.2 (Delta) N-terminal domain. The ACE2 binding affinities of the B.1.617.1 (Kappa) and B.1.617.2 (Delta) receptor-binding domains are comparable to the Wuhan-Hu-1 isolate whereas B.1.617.2+ (Delta+) exhibits markedly reduced affinity.

Reference

https://www.science.org/doi/10.1126/science.abl8506

A regulatory T cell signature distinguishes the immune landscape of COVID-19 patients from those with other respiratory infections

Abstract

Despite recent studies of immunity to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), little is known about how the immune response against SARS-CoV-2 differs from other respiratory infections. The immune signature was compared from hospitalized SARS-CoV-2–infected patients to patients hospitalized prepandemic with influenza or respiratory syncytial virus (RSV). These in-depth profiling indicates that the immune landscape in SARS-CoV-2 patients is largely similar to flu or RSV patients.

Unique to patients infected with SARS-CoV-2 who had the most critical clinical disease were changes in the regulatory T cell (Treg) compartment. A Treg signature including increased frequency, activation status, and migration markers was correlated COVID-19 severity. These findings are relevant as Tregs are considered for therapy to combat the severe inflammation seen in COVID-19 patients. Likewise, having defined the overlapping immune landscapes in SARS-CoV-2, existing knowledge of flu and RSV infections could be leveraged to identify common treatment strategies.

Reference

https://www.science.org/doi/10.1126/sciadv.abj0274

Elevated fecal and serum calprotectin in COVID-19 are not consistent with gastrointestinal symptoms

Abstract

Intestinal epithelial cell damage caused by SARS-CoV-2 infection was thought to be associated with gastrointestinal symptoms and decreased fecal consistency. The association of the gastrointestinal symptoms with the COVID-19-mediated inflammatory response triggered by the gastrointestinal immune system was investigated in this paper. Intestinal inflammation marker fecal calprotectin along with serum calprotectin and other inflammatory markers were measured in COVID-19 cases with and without GI manifestations as well as healthy individuals. Analyses were performed to compare COVID-19 patient subgroups and healthy controls and examine the relationship between fecal and serum calprotectin levels with gastrointestinal symptoms and disease severity. COVID-19 patients ($n = 70$) were found to have markedly elevated median levels of fecal (124.3 vs. 25.0 μg/g; $P < 0/0001$) and serum calprotectin (3500 vs. 1060 ng/mL; $P < 0/0001$) compared with uninfected controls. Fecal and serum calprotectin levels were not significantly different between COVID-19 patients who displayed GI symptoms and those who did not. Compared with other acute phase markers, both fecal and serum calprotectin were superior in identifying COVID-19 patients who progressed to severe illness. Although the progression of COVID-19 disease is marked by an elevation of fecal and serum calprotectin, gastrointestinal symptoms or diarrhea were not correlated with calprotectin increase level.

Reference

https://www.nature.com/articles/s41598-021-01231-4

Publication Date: Nov 08, 2021

Stem cell-based therapy for COVID-19 and ARDS: A systematic review

Abstract

Despite global efforts to establish effective interventions for coronavirus disease 2019 (COVID-19) and its major complications, such as acute respiratory distress syndrome (ARDS), the treatment remains mainly supportive. Hence, identifying an effective and safe therapy for severe COVID-19 is critical for saving lives. A significant number of cell-based therapies have been through clinical investigation. In this study, a systematic review of clinical studies was performed for investigating different types of stem cells as treatments for COVID-19 and ARDS to evaluate the safety and potential efficacy of cell therapy. The literature search was performed using PubMed, Embase, and Scopus. Among the 29 studies, there were eight case reports, five Phase I clinical trials, four pilot studies, two Phase II clinical trials, one cohort, and one case series. Among the clinical studies, 21 studies used cell therapy to treat COVID-19, while eight studies investigated cell therapy as a treatment for ARDS. Most of these (75%) used mesenchymal stem cells (MSCs) to treat COVID-19 and ARDS. Findings from the analyzed articles indicate a positive impact of stem cell therapy on crucial immunological and inflammatory processes that lead to lung injury in COVID-19 and ARDS patients. Additionally, among the studies, there were no reported deaths causally linked to cell therapy. In addition to standard care treatments concerning COVID-19 management, there has been supportive evidence towards adjuvant therapies to reduce mortality rates and improve recovery of care treatment. Therefore, MSCs treatment could be considered a potential candidate for adjuvant therapy in moderate-to-severe COVID-19 cases and compassionate use.

Reference

https://www.nature.com/articles/s41536-021-00181-9

Cross-reactivity of antibodies from non-hospitalized COVID-19 positive individuals against the native, B.1.351, B.1.617.2, and P.1 SARS-CoV-2 spike proteins

Abstract

SARS-CoV-2 variants of concern (VOCs) have emerged worldwide, with implications on the spread of the pandemic. Characterizing the cross-reactivity of antibodies against these VOCs is necessary to understand the humoral response of non-hospitalized individuals previously infected with SARS-CoV-2, a population that remains understudied. Thirty-two SARS-CoV-2-positive (PCR-confirmed) and non-hospitalized Canadian adults were enrolled 14–21 days post-diagnosis in 2020, before the emergence of the B.1.351 (also known as Beta), B.1.617.2 (Delta) and P.1 (Gamma) VOCs. Sera were collected 4 and 16 weeks post-diagnosis. Antibody levels and pseudo-neutralization of the ectodomain of SARS-CoV-2 spike protein/human ACE-2 receptor interaction were analyzed with native, B.1.351, B.1.617.2 and P.1 variant spike proteins. Despite a lower response observed for the variant spike proteins, we report evidence of a sustained humoral response against native, B.1.351, B.1.617.2 and P.1 variant spike proteins among non-hospitalized Canadian adults. Furthermore, this response inhibited the interaction between the spike proteins from the different VOCs and ACE-2 receptor for ≥ 16 weeks post-diagnosis, except for individuals aged 18–49 years who showed no inhibition of the interaction between B.1.617.1 or B.1.617.2 spike and ACE-2. Interestingly, the affinity (KD) measured between the spike proteins (native, B.1.351, B.1.617.2 and P.1) and antibodies elicited in sera of infected and vaccinated (BNT162b2 and ChAdOx1 nCoV-19) individuals was invariant. Relative to sera from vaccine-naïve (and previously infected) individuals, sera from vaccinated individuals had higher antibody levels (as measured with label-free SPR) and more efficiently inhibited the spike–ACE-2 interactions, even among individuals aged 18–49 years, showing the effectiveness of vaccination.

Reference

https://www.nature.com/articles/s41598-021-00844-z

D-Dimer, disease severity, and deaths (3D-study) in patients with COVID-19: A systematic review and meta-analysis of 100 studies

Abstract

Hypercoagulability and the need for prioritizing coagulation markers for prognostic abilities have been highlighted in COVID-19. We aimed to quantify the associations of D-dimer with disease progression in patients with COVID-19. This systematic review and meta-analysis was registered with PROSPERO, CRD42020186661.We included 113 studies in our systematic review, of which 100 records (n = 38,310) with D-dimer data) were considered for meta-analysis. Across 68 unadjusted (n = 26,960) and 39 adjusted studies (n = 15,653) reporting initial D-dimer, a significant association was found in patients with higher D-dimer for the risk of overall disease progression (unadjusted odds ratio (uOR) 3.15; adjusted odds ratio (aOR) 1.64). The time-to-event outcomes were pooled across 19 unadjusted (n = 9743) and 21 adjusted studies (n = 13,287); a strong association was found in patients with higher D-dimers for the risk of overall disease progression (unadjusted hazard ratio (uHR) 1.41; adjusted hazard ratio (aHR) 1.10). The prognostic use of higher D-dimer was found to be promising for predicting overall disease progression (studies 68, area under curve 0.75) in COVID-19. This study showed that higher D-dimer levels provide prognostic information useful for clinicians to early assess COVID-19 patients at risk for disease progression and mortality outcomes. This study, recommends rapid assessment of D-dimer for predicting adverse outcomes in COVID-19.

Reference

Http://www.nature.com/articles/s41598-021-01462-5

Single-cell immunophenotyping of the fetal immune response to maternal SARS-CoV-2 infection in late gestation

Abstract

Background: During the COVID-19 pandemic, thousands of pregnant women have been infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The implications of maternal SARS-CoV-2 infection on fetal and childhood well-being need

to be characterized. We aimed to characterize the fetal immune response to maternal SARS-CoV-2 infection.

Methods: Single-cell RNA-sequencing and T cell receptor sequencing were performed on cord blood mononuclear cells (CBMCs) from newborns of mothers infected with SARS-CoV-2 in the third trimester (cases) or without SARS-CoV-2 infection (controls).

Results: It was identified that widespread gene expression changes in CBMCs from cases, including upregulation of interferon-stimulated genes and major histocompatibility complex genes in CD14+ monocytes, transcriptional changes suggestive of activation of plasmacytoid dendritic cells, and activation and exhaustion of natural killer cells. Lastly, we observed fetal T cell clonal expansion in cases compared to controls.

Conclusions: As none of the infants were infected with SARS-CoV-2, our results suggest that maternal SARS-CoV-2 infection might modulate the fetal immune system in the absence of vertical transmission.

Reference

https://www.nature.com/articles/s41390-021-01793-z

Drug repurposing for coronavirus (SARS-CoV-2) based on gene co-expression network analysis

Abstract

Severe acute respiratory syndrome (SARS) is a highly contagious viral respiratory illness. This illness is spurred on by a coronavirus known as SARS-associated coronavirus (SARS-CoV). SARS was first detected in Asia in late February 2003. The genome of this virus is very similar to the SARS-CoV-2. Therefore, the study of SARS-CoV disease and the identification of effective drugs to treat this disease can be new clues for the treatment of SARS-Cov-2. This study aimed to discover novel potential drugs for SARS-CoV disease in order to treating SARS-Cov-2 disease based on a novel systems biology approach. To this end, gene co-expression network analysis was applied. First, the gene co-expression network was reconstructed for 1441 genes, and then two gene modules were discovered as significant modules. Next, a list of miRNAs and transcription factors that target gene co-expression modules' genes were gathered

from the valid databases, and two sub-networks formed of transcription factors and miRNAs were established. Afterward, the list of the drugs targeting obtained sub-networks' genes was retrieved from the DGIDb database, and two drug-gene and drug-TF interaction networks were reconstructed. Finally, after conducting different network analyses, we proposed five drugs, including FLUOROURACIL, CISPLATIN, SIROLIMUS, CYCLOPHOSPHAMIDE, and METHYLDOPA, as candidate drugs for SARS-CoV-2 coronavirus treatment. Moreover, ten miRNAs including miR-193b, miR-192, miR-215, miR-34a, miR-16, miR-16, miR-92a, miR-30a, miR-7, and miR-26b were found to be significant miRNAs in treating SARS-CoV-2 coronavirus.

Reference

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

Immunogenic and efficacious SARS-CoV-2 vaccine based on resistin-trimerized spike antigen SmT1 and SLA archaeosome adjuvant

Abstract

The huge worldwide demand for vaccines targeting SARS-CoV-2 has necessitated the continued development of novel improved formulations capable of reducing the burden of the COVID-19 pandemic. Herein, we evaluated novel protein subunit vaccine formulations containing a resistin-trimerized spike antigen, SmT1. When combined with sulfated lactosyl archaeol (SLA) archaeosome adjuvant, formulations induced robust antigen-specific humoral and cellular immune responses in mice. Antibodies had strong neutralizing activity, preventing viral spike binding and viral infection. In addition, the formulations were highly efficacious in a hamster challenge model reducing viral load and body weight loss even after a single vaccination. The antigen-specific antibodies generated by our vaccine formulations had stronger neutralizing activity than human convalescent plasma, neutralizing the spike proteins of the B.1.1.7 and B.1.351 variants of concern. As such, our SmT1 antigen along with SLA archaeosome adjuvant comprise a promising platform for the development of efficacious protein subunit vaccine formulations for SARS-CoV-2.

Reference

https://www.nature.com/articles/s41598-021-01363-7

Publication Date: Nov 07, 2021

The majority of SARS-CoV-2-specific antibodies in COVID-19 patients with obesity are autoimmune and not neutralizing

Abstract

Background/objectives: Obesity decreases the secretion of SARS-CoV-2-specific IgG antibodies in the blood of COVID-19 patients. How obesity impacts the quality of the antibodies secreted, however, is not understood. Therefore, the objective of this study is to evaluate the presence of neutralizing versus autoimmune antibodies in COVID-19 patients with obesity.

Subjects/methods: Thirty serum samples from individuals who tested positive for SARS-CoV-2 infection by RT-PCR were collected from inpatient and outpatient settings. Of these, 15 were lean (BMI < 25) and 15 were obese (BMI ≥ 30). Control serum samples were from 30 uninfected individuals, age-, gender-, and BMI-matched, recruited before the current pandemic. Neutralizing and autoimmune antibodies were measured by ELISA. IgG autoimmune antibodies were specific for malondialdehyde (MDA), a marker of oxidative stress and lipid peroxidation, and for adipocyte-derived protein antigens (AD), markers of virus-induced cell death in the obese adipose tissue.

Results: SARS-CoV-2 infection induces neutralizing antibodies in all lean but only in few obese COVID-19 patients. SARS-CoV-2 infection also induces anti-MDA and anti-AD autoimmune antibodies more in lean than in obese patients as compared to uninfected controls. Serum levels of these autoimmune antibodies, however, are always higher in obese versus lean COVID-19 patients. Moreover, because the autoimmune antibodies found in serum samples of COVID-19 patients have been correlated with serum levels of C-reactive protein (CRP), a general marker of inflammation, we also evaluated the association of anti-MDA and anti-AD antibodies with serum CRP and found a positive association between CRP and autoimmune antibodies.

Conclusions: These results highlight the importance of evaluating the quality of the antibody response in COVID-19 patients with obesity, particularly the presence of autoimmune antibodies, and identify biomarkers of self-tolerance breakdown. This is crucial to protect this vulnerable population at higher risk of responding poorly to infection with SARS-CoV-2 than lean controls.

Reference

https://www.nature.com/articles/s41366-021-01016-9

Publication Date: Nov 05, 2021

Characterization of non-adopters of COVID-19 non-pharmaceutical interventions through a national cross-sectional survey to assess attitudes and behaviours

Abstract

Adoption of non-pharmaceutical interventions (NPIs) remains critical to curtail the spread of COVID-19. Using self-reported adherence to NPIs in Canada, assessed through a national cross-sectional survey of 4498 respondents, we aimed to identify and characterize non-adopters of NPIs, evaluating their attitudes and behaviours to understand barriers and facilitators of adoption. A cluster analysis was used to group adopters separately from non-adopters of NPIs. Associations with sociodemographic factors, attitudes towards COVID-19 and the public health response were assessed using logistic regression models comparing non-adopters to adopters. Of the 4498 respondents, 994 (22%) were clustered as non-adopters. Sociodemographic factors significantly associated with the non-adoption cluster were: (1) being male, (2) age 18–34 years, (3) Albertans, (4) lower education level and (5) higher conservative political leaning. Participants who expressed low concern for COVID-19 and distrust towards several institutions had greater odds of being non-adopters. This information characterizes individuals at greatest odds for non-adoption of NPIs to inform targeted marketing interventions.

Reference

https://www.nature.com/articles/s41598-021-01279-2

Diosmectite inhibits the interaction between SARS-CoV-2 and human enterocytes by trapping viral particles, thereby preventing NF-kappaB activation and CXCL10 secretion

Abstract

SARS-CoV-2 enters the intestine by the spike protein binding to angiotensin-converting enzyme 2 (ACE2) receptors in enterocyte apical membranes, leading to diarrhea in

some patients. Early treatment of COVID-19-associated diarrhea could relieve symptoms and limit viral spread within the gastrointestinal (GI) tract. Diosmectite, an aluminomagnesium silicate adsorbent clay with antidiarrheal effects, is recommended in some COVID-19 management protocols. In rotavirus models, diosmectite prevents pathogenic effects by binding the virus and its enterotoxin. We tested the trapping and anti-inflammatory properties of diosmectite in a SARS-CoV-2 model. Trapping effects were tested in Caco-2 cells using spike protein receptor-binding domain (RBD) and heat-inactivated SARS-CoV-2 preparations. Trapping was assessed by immunofluorescence, alone or in the presence of cells. The effect of diosmectite on nuclear factor kappa B (NF-kappaB) activation and CXCL10 secretion induced by the spike protein RBD and heat-inactivated SARS-CoV-2 were analyzed by Western blot and ELISA, respectively. Diosmectite bound the spike protein RBD and SARS-CoV-2 preparation, and inhibited interaction of the spike protein RBD with ACE2 receptors on the Caco-2 cell surface. Diosmectite exposure also inhibited NF-kappaB activation and CXCL10 secretion. These data provide direct evidence that diosmectite can bind SARS-CoV-2 components and inhibit downstream inflammation, supporting a mechanistic rationale for consideration of diosmectite as a management option for COVID-19-associated diarrhea.

Reference

https://www.nature.com/articles/s41598-021-01217-2

A high-throughput pipeline for design and selection of peptides targeting the SARS-Cov-2 Spike protein

Abstract

Rapid design, screening, and characterization of biorecognition elements (BREs) is essential for the development of diagnostic tests and antiviral therapeutics needed to combat the spread of viruses such as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). To address this need, a high-throughput pipeline was developed combining *in silico* design of a peptide library specific for SARS-CoV-2 spike (S) protein and microarray screening to identify binding sequences. The optimized microarray platform allowed the simultaneous screening of ~ 2.5 k peptides and rapid identification of binding sequences resulting in selection of four peptides with nanomolar affinity to the

SARS-CoV-2 S protein. Finally, it was demonstrated that successful integration of one of the top peptides into an electrochemical sensor with a clinically relevant limit of detection for S protein in spiked saliva. These results demonstrate the utility of this novel pipeline for the selection of peptide BREs in response to the SARS-CoV-2 pandemic, and the broader application of such a platform in response to future viral threats.

Reference

https://www.nature.com/articles/s41598-021-01225-2

SARS-CoV-2 Delta variant excels at membrane fusion, but not immune evasion

Abstract

The SARS-CoV-2 Delta variant has become the dominant strain worldwide. It is around twice as transmissible as its ancestral strain, with a shorter incubation period and higher viral load during infection. Now, Bing Chen and colleagues show that mutations in spike protein of Delta allow for faster membrane fusion than Alpha, Beta, Gamma and Kappa variants, and that Delta is more efficient at infecting cells with very low expression of the ACE2 entry receptor. However, the mutations found in the Delta variant had less impact on its sensitivity to neutralizing antibodies compared to those of the Gamma and Kappa variants. Neutralizing antibodies predominantly target the N-terminal domain (NTD) or the receptor binding domain (RBD) of the spike protein. The authors found different arrangements of the antigenic surface of the NTD in the different variants, but only local changes in the RBD, indicating that therapeutic antibodies or universal vaccines should be targeted at the latter.

Reference

https://www.nature.com/articles/s41577-021-00654-4

Post-exposure Lopinavir-Ritonavir Prophylaxis versus Surveillance for Individuals Exposed to SARS-CoV-2: The COPEP Pragmatic Open-Label, Cluster Randomized Trial

Abstract

Background: Since the beginning of the COVID-19 pandemic, no direct antiviral treatment is effective as post-exposure prophylaxis (PEP). Lopinavir/ritonavir (LPV/r) was repurposed as a potential PEP agent against COVID-19.

Methods: We conducted a pragmatic open-label, parallel, cluster-randomised superiority trial in four sites in Switzerland and Brazil between March 2020 to March 2021. Clusters were randomised to receive LPV/r PEP (400/100 mg) twice daily for 5 days or no PEP (surveillance). Exposure to SARS-CoV-2 was defined as a close contact of >15 minutes in <2 metres distance or having shared a closed space for ≥2 hours with a person with confirmed SARS-CoV-2 infection. The primary outcome is the occurrence of COVID-19 defined by a SARS-CoV-2 infection (positive oropharyngeal SARS-CoV-2 PCR and/or a seroconversion) and ≥1 compatible symptom within 21 days post-enrolment. ClinicalTrials.gov (Identifier: NCT04364022); Swiss National Clinical Trial Portal: SNCTP 000003732.

Findings: Of 318 participants, 157 (49.4%) were women; median age was 39 (interquartile range, 28-50) years. A total of 209 (179 clusters) participants were randomised to LPV/r PEP and 109 (95 clusters) to surveillance. Baseline characteristics were similar, with the exception of baseline SARS-CoV-2 PCR positivity, which was 3-fold more frequent in the LPV/r arm (34/209 [16.3%] vs 6/109 [5.5%], respectively). During 21-day follow-up, 48/318 (15.1%) participants developed COVID-19: 35/209 (16.7%) in the LPV/r group and 13/109 (11.9%) in the surveillance group (unadjusted hazard ratio 1.44; 95% CI, 0.76-2.73). In the primary endpoint analysis, which was adjuted for baseline imbalance, the hazard ratio for developing COVID-19 in the LPV/r group vs surveillance was 0.60 (95% CI, 0.29-1.26; p =0.18).

Interpretation: The role of LPV/r as PEP for COVID-19 remains unanswered. Although LPV/r over 5 days did not significantly reduce the incidence of COVID-19 in exposed individuals, we observed a change in the directionality of the effect in favour of LPV/r

after adjusting for baseline imbalance. LPV/r for this indication merits further testing against SARS-CoV-2 in clinical trials.

Reference

https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00469-7/fulltext

Publication Date: Nov 04, 2021

Potential global impacts of alternative dosing regimen and rollout options for the ChAdOx1 nCoV-19 vaccine

Abstract

The high efficacy, low cost, and long shelf-life of the ChAdOx1 nCoV-19 vaccine positions it well for use in in diverse socioeconomic settings. Using data from clinical trials, an individual-based model was constructed to predict its 6-month population-level impact. Probabilistic sensitivity analyses evaluated the importance of epidemiological, demographic and logistical factors on vaccine effectiveness. Rollout at various levels of availability and delivery speed, conditional on vaccine efficacy profiles (efficacy of each dose and interval between doses) were explored in representative countries. We highlight how expedient vaccine delivery to high-risk groups is critical in mitigating COVID-19 disease and mortality. In scenarios where the availability of vaccine is insufficient for high-risk groups to receive two doses, administration of a single dose of is optimal, even when vaccine efficacy after one dose is just 75% of the two doses. These findings can help inform allocation strategies particularly in areas constrained by availability.

Reference

https://www.nature.com/articles/s41467-021-26449-8

Strong immunogenicity of heterologous prime-boost immunizations with the experimental vaccine GRAd-COV2 and BNT162b2 or ChAdOx1-nCOV19

Abstract

Here, the humoral and cellular immune response was reported in eight volunteers who autonomously chose to adhere to the Italian national COVID-19 vaccination campaign

more than 3 months after receiving a single-administration GRAd-COV2 vaccine candidate in the context of the phase-1 clinical trial. We observed a clear boost of both binding/neutralizing antibodies as well as T-cell responses upon receipt of the heterologous BNT162b2 or ChAdOx1-nCOV19 vaccines. These results, despite the limitation of the small sample size, support the concept that a single dose of an adenoviral vaccine may represent an ideal tool to effectively prime a balanced immune response, which can be boosted to high levels by a single dose of a different vaccine platform.

Reference

https://www.nature.com/articles/s41467-021-26449-8

Comparison of viral RNA–host protein interactomes across pathogenic RNA viruses informs rapid antiviral drug discovery for SARS-CoV-2

Abstract

In contrast to the extensive research about viral protein–host protein interactions that has revealed major insights about how RNA viruses engage with host cells during infection, few studies have examined interactions between host factors and viral RNAs (vRNAs). Here, we profiled vRNA–host protein interactomes for three RNA virus pathogens (SARS-CoV-2, Zika, and Ebola viruses) using ChIRP-MS. Comparative interactome analyses discovered both common and virus-specific host responses and vRNA-associated proteins that variously promote or restrict viral infection. In particular, SARS-CoV-2 binds and hijacks the host factor IGF2BP1 to stabilize vRNA and augment viral translation. Our interactome-informed drug repurposing efforts identified several FDA-approved drugs (e.g., Cepharanthine) as broad-spectrum antivirals in cells and hACE2 transgenic mice. A co-treatment comprising Cepharanthine and Trifluoperazine was highly potent against the newly emerged SARS-CoV-2 B.1.351 variant. Thus, our study illustrates the scientific and medical discovery utility of adopting a comparative vRNA–host protein interactome perspective.

Reference

https://www.nature.com/articles/s41422-021-00581-y

High sensitivity-low cost detection of SARS-CoV-2 by two steps end point RT-PCR with agarose gel electrophoresis visualization

Abstract

More than one year since Coronavirus disease 2019 (COVID-19) pandemic outbreak, the gold standard technique for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) detection is still the RT-qPCR. This is a limitation to increase testing capacities, particularly at developing countries, as expensive reagents and equipment are required. We developed a two steps end point RT-PCR reaction with SARS-CoV-2 Nucleocapsid (N) gene and Ribonuclease P (RNase P) specific primers where viral amplicons were verified by agarose gel electrophoresis. We carried out a clinical performance and analytical sensitivity evaluation for this two-steps end point RT-PCR method with 242 nasopharyngeal samples using the CDC RT-qPCR protocol as a gold standard technique. With a specificity of 95.8%, a sensitivity of 95.1%, and a limit of detection of 20 viral RNA copies/uL, this two steps end point RT-PCR assay is an affordable and reliable method for SARS-CoV-2 detection. This protocol would allow to extend COVID-19 diagnosis to basic molecular biology laboratories with a potential positive impact in surveillance programs at developing countries.

Reference

https://www.nature.com/articles/s41467-021-26449-8

Distinct SARS-CoV-2 antibody reactivity patterns elicited by natural infection and mRNA vaccination

Abstract

We analyzed data from two ongoing COVID-19 longitudinal serological surveys in Orange County, CA., between April 2020 and March 2021. A total of 8476 finger stick blood specimens were collected before and after a vaccination campaign. IgG levels were determined using a multiplex antigen microarray containing antigens from SARS-CoV-2, SARS, MERS, Common CoV, and Influenza. Twenty-six percent of specimens from unvaccinated Orange County residents in December 2020 were SARS-CoV-2 seropositive; out of 852 seropositive individuals 77 had symptoms and 9 sought medical care. The antibody response was predominantly against nucleocapsid (NP), full length,

and S2 domain of spike. Anti-receptor binding domain (RBD) reactivity was low and not cross-reactive against SARS S1 or SARS RBD. A vaccination campaign at the University of California Irvine Medical Center (UCIMC) started on December, 2020 and 6724 healthcare workers were vaccinated within 3 weeks. Seroprevalence increased from 13% pre-vaccination to 79% post-vaccination in January, 93% in February, and 99% in March. mRNA vaccination induced higher antibody levels than natural exposure, especially against the RBD domain and cross-reactivity against SARS RBD and S1 was observed. Nucleocapsid protein antibodies can be used to distinguish vaccinees to classify pre-exposure to SARS-CoV-2 Previously infected individuals developed higher antibody titers to the vaccine than non pre-exposed individuals. Hospitalized patients in intensive care with severe disease reach significantly higher antibody levels than mild cases, but lower antibody levels compared to the vaccine. These results indicate that mRNA vaccination rapidly induces a much stronger and broader antibody response than SARS-CoV-2 infection.

Reference

https://www.nature.com/articles/s41541-021-00396-3

Within-host evolution of SARS-CoV-2 in an immunosuppressed COVID-19 patient as a source of immune escape variants

Abstract

The origin of SARS-CoV-2 variants of concern remains unclear. Here, it was tested whether intra-host virus evolution during persistent infections could be a contributing factor by characterizing the long-term SARS-CoV-2 infection dynamics in an immunosuppressed kidney transplant recipient. Applying RT-qPCR and next-generation sequencing (NGS) of sequential respiratory specimens, we identify several mutations in the viral genome late in infection. We demonstrate that a late viral isolate exhibiting genome mutations similar to those found in variants of concern first identified in UK, South Africa, and Brazil, can escape neutralization by COVID-19 antisera. Moreover, infection of susceptible mice with this patient's escape variant elicits protective immunity against re-infection with either the parental virus and the escape variant, as well as high neutralization titers against the alpha and beta SARS-CoV-2 variants, B.1.1.7 and B.1.351, demonstrating a considerable immune control against such variants of

concern. Upon lowering immunosuppressive treatment, the patient generated spike-specific neutralizing antibodies and resolved the infection. Our results suggest that immunocompromised patients could be a source for the emergence of potentially harmful SARS-CoV-2 variants.

Reference

https://www.nature.com/articles/s41467-021-26602-3

Estimating the impact of virus testing strategies on the COVID-19 case fatality rate using fixed-effects models

Abstract

Data was analyzed from two ongoing COVID-19 longitudinal serological surveys in Orange County, CA., between April 2020 and March 2021. A total of 8476 finger stick blood specimens were collected before and after a vaccination campaign. IgG levels were determined using a multiplex antigen microarray containing antigens from SARS-CoV-2, SARS, MERS, Common CoV, and Influenza. Twenty-six percent of specimens from unvaccinated Orange County residents in December 2020 were SARS-CoV-2 seropositive; out of 852 seropositive individuals 77 had symptoms and 9 sought medical care. The antibody response was predominantly against nucleocapsid (NP), full length, and S2 domain of spike. Anti-receptor binding domain (RBD) reactivity was low and not cross-reactive against SARS S1 or SARS RBD. A vaccination campaign at the University of California Irvine Medical Center (UCIMC) started on December, 2020 and 6724 healthcare workers were vaccinated within 3 weeks. Seroprevalence increased from 13% pre-vaccination to 79% post-vaccination in January, 93% in February, and 99% in March. mRNA vaccination induced higher antibody levels than natural exposure, especially against the RBD domain and cross-reactivity against SARS RBD and S1 was observed. Nucleocapsid protein antibodies can be used to distinguish vaccinees to classify pre-exposure to SARS-CoV-2 Previously infected individuals developed higher antibody titers to the vaccine than non pre-exposed individuals. Hospitalized patients in intensive care with severe disease reach significantly higher antibody levels than mild cases, but lower antibody levels compared to the vaccine. These results indicate that mRNA vaccination rapidly induces a much stronger and broader antibody response than SARS-CoV-2 infection.

Reference

https://www.nature.com/articles/s41598-021-01034-7

Potential global impacts of alternative dosing regimen and rollout options for the ChAdOx1 nCoV-19 vaccine

Abstract

The high efficacy, low cost, and long shelf-life of the ChAdOx1 nCoV-19 vaccine positions it well for use in in diverse socioeconomic settings. Using data from clinical trials, an individual-based model was constructed to predict its 6-month population-level impact. Probabilistic sensitivity analyses evaluated the importance of epidemiological, demographic and logistical factors on vaccine effectiveness. Rollout at various levels of availability and delivery speed, conditional on vaccine efficacy profiles (efficacy of each dose and interval between doses) were explored in representative countries. It was highlighted how expedient vaccine delivery to high-risk groups is critical in mitigating COVID-19 disease and mortality. In scenarios where the availability of vaccine is insufficient for high-risk groups to receive two doses, administration of a single dose of is optimal, even when vaccine efficacy after one dose is just 75% of the two doses. These findings can help inform allocation strategies particularly in areas constrained by availability.

Reference

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performance and analytical sensitivity evaluation for this two-steps end point RT-PCR method with 242 nasopharyngeal samples using the CDC RT-qPCR protocol as a gold standard technique. With a specificity of 95.8%, a sensitivity of 95.1%, and a limit of detection of 20 viral RNA copies/uL, this two steps end point RT-PCR assay is an affordable and reliable method for SARS-CoV-2 detection. This protocol would allow to extend COVID-19 diagnosis to basic molecular biology laboratories with a potential positive impact in surveillance programs at developing countries.

Reference

https://www.nature.com/articles/s41598-021-00900-8

Comparison of viral RNA–host protein interactomes across pathogenic RNA viruses informs rapid antiviral drug discovery for SARS-CoV-2

Abstract

In contrast to the extensive research about viral protein–host protein interactions that has revealed major insights about how RNA viruses engage with host cells during infection, few studies have examined interactions between host factors and viral RNAs (vRNAs). Here, we profiled vRNA–host protein interactomes for three RNA virus pathogens (SARS-CoV-2, Zika, and Ebola viruses) using ChIRP-MS. Comparative interactome analyses discovered both common and virus-specific host responses and vRNA-associated proteins that variously promote or restrict viral infection. In particular, SARS-CoV-2 binds and hijacks the host factor IGF2BP1 to stabilize vRNA and augment viral translation. Our interactome-informed drug repurposing efforts identified several FDA-approved drugs (e.g., Cepharanthine) as broad-spectrum antivirals in cells and hACE2 transgenic mice. A co-treatment comprising Cepharanthine and Trifluoperazine was highly potent against the newly emerged SARS-CoV-2 B.1.351 variant. Thus, our study illustrates the scientific and medical discovery utility of adopting a comparative vRNA–host protein interactome perspective.

Reference

https://www.nature.com/articles/s41422-021-00581-y

Correlation of SARS-CoV-2-breakthrough infections to time-from-vaccine

Abstract

The short-term effectiveness of a two-dose regimen of the BioNTech/Pfizer mRNA BNT162b2 severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine was widely demonstrated. However, long term effectiveness is still unknown. Leveraging the centralized computerized database of Maccabi Healthcare Services (MHS), we assessed the correlation between time-from-vaccine and incidence of breakthrough infection between June 1 and July 27, the date of analysis. After controlling for potential confounders as age and comorbidities, we found a significant 1.51 fold (95% CI, 1.38–1.66) increased risk for infection for early vaccinees compared to those vaccinated later that was similar across all ages groups. The increased risk reached 2.26- fold (95% CI, 1.80–3.01) when comparing those who were vaccinated in January to those vaccinated in April. This preliminary finding of vaccine waning as a factor of time from vaccince should prompt further investigations into long-term protection against different strains.

Reference

https://www.nature.com/articles/s41467-021-26672-3

REPORT

Publication Date: Nov 04, 2021

Rapid assessment of SARS-CoV-2 evolved variants using virus-like particles

Efforts to determine why new SARS-CoV-2 variants demonstrate improved fitness have been limited to analyzing mutations in the spike (S) protein using S-pseudotyped particles. Here we show that SARS-CoV-2 virus-like particles (SC2-VLPs) can package and deliver exogenous transcripts, enabling analysis of mutations within all structural proteins and at multiple steps in the viral life cycle. In SC2-VLPs, four nucleocapsid (N) mutations found universally in more-transmissible variants independently increased mRNA delivery and expression by ~10-fold, and in a reverse genetics model, S202R and R203M each produced >50-fold more virus. SC2-VLPs provide a platform for rapid testing of viral variants outside a biosafety level 3 setting and demonstrate N mutations and particle assembly to be mechanisms that could explain the increased spread of variants, including Delta (R203M).

Reference

https://www.science.org/doi/10.1126/science.abl6184