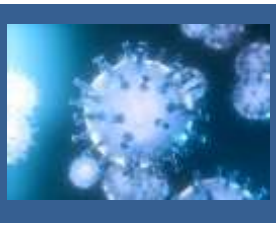
COVID-19

Nov 11 – 17, 2021



RESEARCH PUBLICATIONS

Publication Date: Nov 17, 2021

Sarilumab in adults hospitalised with moderate-to-severe COVID-19 pneumonia (CORIMUNO-SARI-1): An open-label randomised controlled trial

Abstract

Background: Patients with COVID-19 pneumonia can have increased inflammation and elevated cytokines, including interleukin (IL)-6, which might be deleterious. Thus, sarilumab, a high-affinity anti-IL-6 receptor antibody, might improve the outcome of patients with moderate-to-severe COVID-19 pneumonia.

Methods: A multicentric, open-label, Bayesian randomised, adaptive, phase 2/3 clinical trial was done, nested within the CORIMUNO-19 cohort, to test a superiority hypothesis. Patients 18 years or older hospitalised with COVID-19 in six French centres, requiring at least 3L/min of oxygen but without ventilation assistance and a WHO Clinical Progression Scale [CPS] score of 5 were enrolled. Patients were randomly assigned (1:1) *via* a web-based system, according to a randomisation list stratified on centre and with blocks randomly selected among 2 and 4, to receive usual care plus 400 mg of sarilumab intravenously on day 1 and on day 3 if clinically indicated (sarilumab group) or usual care alone (usual care group). Primary outcomes were the proportion of patients with WHO-CPS scores greater than 5 on the 10-point scale on day 4 and survival without invasive or non-invasive ventilation at day 14. This completed trial is closed to new participants and is registered with ClinicalTrials.gov, NCT04324073.

Findings: 165 Patients were recruited from March 27 to April 6, 2020, and 148 patients were randomised (68 patients to the sarilumab group and 80 to the usual care group) and followed up for 90 days. Median age was 61·7 years [IQR 53·0–71·1] in the sarilumab group and 62·8 years [56·0–71·7] in the usual care group. In the sarilumab

group 49 (72%) of 68 were men and in the usual care group 59 (78%) of 76 were men. Four patients in the usual care group withdrew consent and were not analysed. 18 (26%) of 68 patients in the sarilumab group had a WHO-CPS score greater than 5 at day 4 versus 20 (26%) of 76 in the usual care group (median posterior absolute risk difference 0·2%; 90% credible interval [CrI] −11·7 to 12·2), with a posterior probability of absolute risk difference greater than 0 of 48·9%. At day 14, 25 (37%) patients in the sarilumab and 26 (34%) patients in the usual care group needed ventilation or died, (median posterior hazard ratio [HR] 1·10; 90% CrI 0·69–1·74) with a posterior probability HR greater than 1 of 37·4%. Serious adverse events occurred in 27 (40%) patients in the sarilumab group and 28 (37%) patients in the usual care group (p=0·73).

Interpretation: Sarilumab treatment did not improve early outcomes in patients with moderate-to-severe COVID-19 pneumonia. Further studies are warranted to evaluate the effect of sarilumab on long-term survival.

Reference

https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(21)00315-5/fulltext

Safety, immunogenicity, and efficacy of a COVID-19 vaccine (NVX-CoV2373) co-administered with seasonal influenza vaccines: An exploratory substudy of a randomised, observer-blinded, placebo-controlled, phase 3 trial

Abstract

Background: The safety and immunogenicity profile of COVID-19 vaccines when administered concomitantly with seasonal influenza vaccines have not yet been reported. It was therefore aimed to report the results of a substudy within a phase 3 UK trial, by evaluating the safety, immunogenicity, and efficacy of NVX-CoV2373 when co-administered with licensed seasonal influenza vaccines.

Methods: A planned exploratory substudy was done as part of the randomised, observer-blinded, placebo-controlled, phase 3 trial of the safety and efficacy of the COVID-19 vaccine (NVX-CoV2373) by co-administrating the influenza vaccine at four study hospitals in the UK. Approximately, the first 400 participants meeting the main study entry criteria—with no contraindications to influenza vaccination—were invited to join the substudy. Participants of the main study were randomly assigned (1:1) to

receive two intramuscular injections of either NVX-CoV2373 (5 µg) or placebo (normal saline) 21 days apart; participants enrolled into the substudy were co-vaccinated with a single (0·5 mL) intramuscular, age-appropriate (quadrivalent influenza cell-based vaccine [Flucelvax Quadrivalent; Seqirus UK, Maidenhead] for those aged 18–64 years and adjuvanted trivalent influenza vaccine [Fluad; Seqirus UK, Maidenhead] for those ≥65 years), licensed, influenza vaccine on the opposite deltoid to that of the first study vaccine dose or placebo. The influenza vaccine was administered in an open-label manner and at the same time as the first study injection. Reactogenicity was evaluated via an electronic diary for 7 days after vaccination in addition to monitoring for unsolicited adverse events, medically attended adverse events, and serious adverse events. Immunogenicity was assessed with influenza haemagglutination inhibition and SARS-CoV-2 anti-spike protein IgG assays. Vaccine efficacy against PCR-confirmed, symptomatic COVID-19 was assessed in participants who were seronegative at baseline, received both doses of study vaccine or placebo, had no major protocol deviations affecting the primary endpoint, and had no confirmed cases of symptomatic COVID-19 from the first dose until 6 days after the second dose (per-protocol efficacy population). Immunogenicity was assessed in participants who received scheduled two doses of study vaccine, had a baseline sample and at least one post-vaccination sample, and had no major protocol violations before unmasking (per-protocol immunogenicity population). Reactogenicity was analysed in all participants who received at least one dose of NVX-CoV2373 or placebo and had data collected for reactogenicity events. Safety was analysed in all participants who received at least one dose of NVX-CoV2373 or placebo. Comparisons were made between participants of the substudy and the main study (who were not co-vaccinated for influenza). This study is registered with ClinicalTrials.gov, number NCT04583995.

Findings: Between Sept 28, 2020, and Nov 28, 2020, a total of 15 187 participants were randomised into the main phase 3 trial, of whom 15 139 received treatment (7569 received dose one of NVX-CoV2373 and 7570 received dose one of placebo). 431 participants were co-vaccinated with a seasonal influenza vaccine in the substudy (217 received NVX-CoV2373 plus the influenza vaccine and 214 received placebo plus the influenza vaccine). In general, the substudy participants were younger, more racially diverse, and had fewer comorbid conditions than those in the main study. Reactogenicity events were more common in the co-administration group than in the

NVX-CoV2373 alone group: tenderness (113 [64·9%] of 174 vs 592 [53·3%] of 1111) or pain (69 [39·7%] vs 325 [29·3%]) at injection site, fatigue (48 [27·7%] vs 215 [19·4%]), and muscle pain (49 [28·3%] vs 237 [21·4%]). Incidences of unsolicited adverse events, treatment-related medically attended adverse events, and serious adverse events were low and balanced between the co-administration group and the NVX-CoV2373 alone group. No episodes of anaphylaxis or deaths were reported within the substudy. Co-administration resulted in no change to influenza vaccine immune response although a reduction in antibody responses to the NVX-CoV2373 vaccine was noted. NVX-CoV2373 vaccine efficacy in the substudy (ie, participants aged 18 to <65 years) was 87·5% (95% CI −0·2 to 98·4) and in the main study was 89·8% (95% CI 79·7–95·5).

Interpretation: To our knowledge, this substudy is the first to show the safety, immunogenicity, and efficacy profile of a COVID-19 vaccine when co-administered with seasonal influenza vaccines. Our results suggest concomitant vaccination might be a viable immunisation strategy.

Reference

https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00409-4/fulltext

DEspR^{high} neutrophils are associated with critical illness in COVID-19

Abstract

SARS-CoV-2 infection results in a spectrum of outcomes from no symptoms to widely varying degrees of illness to death. A better understanding of the immune response to SARS-CoV-2 infection and subsequent, often excessive, inflammation may inform treatment decisions and reveal opportunities for therapy. Immune cell subpopulations and their associations with clinical parameters were studied in a cohort of 26 patients with COVID-19. Following informed consent, blood samples were collected from hospitalized patients with COVID-19 within 72 h of admission. Flow cytometry was used to analyze white blood cell subpopulations. Plasma levels of cytokines and chemokines were measured using ELISA. Neutrophils undergoing neutrophil extracellular traps (NET) formation were evaluated in blood smears. The immunophenotype of patients with COVID-19 was examined in comparison to that of SARS-CoV-2 negative controls. A novel subset of pro-inflammatory neutrophils expressing a high level of dual endothelin-1 and VEGF signal peptide-activated receptor (DEspR) at the cell surface

was found to be associated with elevated circulating CCL23, increased NETosis, and critical-severity COVID-19 illness. The potential to target this subpopulation of neutrophils to reduce secondary tissue damage caused by SARS-CoV-2 infection warrants further investigation.

Reference

https://www.nature.com/articles/s41598-021-01943-7

Metaviromic identification of discriminative genomic features in SARS-CoV-2 using machine learning

Abstract

The COVID-19 pandemic caused by SARS-CoV-2 has become a major threat across the globe. Here, machine learning approaches were developed to identify key pathogenic regions in coronavirus genomes. 7,562,625 Models were trained and evaluated on 3,665 genomes including SARS-CoV-2, MERS-CoV, SARS-CoV and other coronaviruses of human and animal origins to return quantitative and biologically interpretable signatures at nucleotide and amino acid resolutions. Hotspots were identified across the SARS-CoV-2 genome including previously unappreciated features in spike, RdRp and other proteins. Finally, pathogenicity genomic profiles were integrated with B cell and T cell epitope predictions for enrichment of sequence targets to help guide vaccine development. These results provide a systematic map of predicted pathogenicity in SARS-CoV-2 that incorporates sequence, structural and immunological features, providing an unbiased collection of genetic elements for functional studies. This metavirome-based framework can also be applied for rapid characterization of new coronavirus strains or emerging pathogenic viruses.

Reference

https://www.cell.com/patterns/fulltext/S2666-3899(21)00281-6

Reduced antibody activity against SARS-CoV-2 B.1.617.2 Delta virus in serum of mRNA-vaccinated patients receiving Tumor Necrosis Factor-*α* inhibitors

Abstract

Background: Although vaccines effectively prevent COVID-19 in healthy individuals, they appear less immunogenic in individuals with chronic inflammatory diseases (CID) or receiving chronic immunosuppression therapy.

Methods: Here, a cohort of 77 CID patients were assessed and treated as monotherapy with chronic immunosuppressive drugs for antibody responses in serum against historical and variant SARS-CoV-2 viruses after immunization with the BNT162b2 mRNA vaccine.

Findings: Longitudinal analysis showed the greatest reductions in neutralizing antibodies and Fc effector functions capacity in individuals treated with TNF-α inhibitors (TNFi), and this pattern appeared worse against B.1.617.2 Delta virus. Within five months of vaccination, serum neutralizing titers of all TNFi-treated patients tested fell below the presumed threshold correlate for antibody-mediated protection. However, TNFi-treated patients receiving a third mRNA vaccine dose boosted their serum neutralizing antibody titers by more than 16-fold.

Conclusions: Thus, vaccine boosting or administration of long-acting prophylaxis (e.g., monoclonal antibodies) likely will be required to prevent SARS-CoV-2 infection in this susceptible population.

Reference

https://www.cell.com/med/fulltext/S2666-6340(21)00378-0

Immune system cells from COVID-19 patients display compromised mitochondrial-nuclear expression co-regulation and rewiring toward glycolysis

Abstract

Mitochondria are pivotal for bioenergetics, as well as in cellular response to viral infections. Nevertheless, their role in COVID-19 was largely overlooked. Here, available bulk RNA-seq datasets were analyzed from COVID-19 patients and corresponding healthy controls (three blood datasets, N = 48 healthy, 119 patients; two respiratory

tract datasets, N = 157 healthy, 524 patients). It was found that significantly reduced mtDNA gene expression in blood, but not in respiratory tract samples from patients. Next, analysis of eight single-cells RNA-seq datasets from peripheral blood mononuclear cells, nasopharyngeal samples, and Bronchoalveolar lavage fluid (N = 1,192,243 cells), revealed significantly reduced mtDNA gene expression especially in immune system cells from patients. This is associated with elevated expression of nuclear DNA-encoded OXPHOS subunits, suggesting compromised mitochondrial-nuclear co-regulation. This, together with elevated expression of ROS-response genes and glycolysis enzymes in patients, suggest rewiring toward glycolysis, thus generating beneficial conditions for SARS-CoV-2 replication. The findings underline the centrality of mitochondrial dysfunction in COVID-19.

Reference

https://www.cell.com/iscience/fulltext/S2589-0042(21)01442-5

Fluvastatin mitigates SARS-CoV-2 infection in human lung cells

Abstract

Clinical data of patients suffering from COVID-19 indicates that statin therapy, used to treat hypercholesterolemia, is associated with a better disease outcome. Whether statins directly affect virus replication or influence the clinical outcome through modulation of immune responses is unknown. It was therefore investigated that the effect of statins on SARS-CoV-2 infection in human lung cells and found that only fluvastatin inhibited low and high pathogenic coronaviruses *in vitro* and *ex vivo* in a dose-dependent manner. Quantitative proteomics revealed that fluvastatin and other tested statins modulated the cholesterol synthesis pathway without altering innate antiviral immune responses in infected lung epithelial cells. However, fluvastatin treatment specifically downregulated proteins that modulate protein translation and viral replication. Collectively, these results support the notion that statin therapy poses no additional risk to individuals exposed to SARS-CoV-2 and that fluvastatin has a moderate beneficial effect on SARS-CoV-2 infection of human lung cells.

Reference

https://www.cell.com/iscience/fulltext/S2589-0042(21)01440-1

Non-propagative human parainfluenza virus type 2 nasal vaccine robustly protects the upper and lower airways against SARS-CoV-2

Abstract

An intranasal vaccine was developed against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) using the replication-incompetent human parainfluenza virus type 2 (hPIV2) vector BC-PIV, which can deliver ectopic gene as stable RNA and ectopic protein on the envelope. BC-PIV expressing the full-length prefusion-stabilized spike gene (K986P/V987P) of SARS-CoV-2, S-2PM, possessed a corona-like viral envelope. Intranasal vaccination of mice with BC-PIV/S-2PM induced high levels of neutralizing immunoglobulin G (IgG) and mucosal IgA antibodies against the spike protein. Although BC-PIV showed hemagglutinating activity, BC-PIV/S-2PM lacked such activity, in accordance with the presence of the massive spike protein on the viral surface. Furthermore, single-dose intranasal vaccination of hamsters with BC-PIV/S-2PM completely protected the lungs from SARS-CoV-2 at 11-week post-immunization, and boost vaccination two weeks before the challenge conferred virtually complete protection of the nasal turbinates against SARS-CoV-2. Thus, this chimeric hPIV2/spike intranasal vaccine is a promising vaccine candidate for SARS-CoV-2 to curtail virus transmission.

Reference

https://www.cell.com/iscience/fulltext/S2589-0042(21)01350-X

Publication Date: Nov 16, 2021

Organ-specific genome diversity of replication-competent SARS-CoV-2

Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is not always confined to the respiratory system, as it impacts people on a broad clinical spectrum from asymptomatic to severe systemic manifestations resulting in death. Further, accumulation of intra-host single nucleotide variants during prolonged SARS-CoV-2 infection may lead to emergence of variants of concern (VOCs). Still, information on virus infectivity and intra-host evolution across organs is sparse. A detailed virological analysis of thirteen postmortem coronavirus disease 2019 (COVID-19) cases was

reported that provides proof of viremia and presence of replication-competent SARS-CoV-2 in extrapulmonary organs of immunocompromised patients, including heart, kidney, liver, and spleen (NCT04366882). In parallel, organ-specific SARS-CoV-2 genome diversity and mutations of concern N501Y, T1027I, and Y453F were identified, while the patient had died long before reported emergence of VOCs. These mutations appear in multiple organs and replicate in Vero E6 cells, highlighting their infectivity. Finally, we show two stages of fatal disease evolution based on disease duration and viral loads in lungs and plasma. The results provide insights about the pathogenesis and intra-host evolution of SARS-CoV-2 and show that COVID-19 treatment and hygiene measures need to be tailored to specific needs of immunocompromised patients, even when respiratory symptoms cease.

Reference

https://www.nature.com/articles/s41467-021-26884-7

SARS-CoV-2 infection and replication in human gastric organoids

Abstract

COVID-19 typically manifests as a respiratory illness, but several clinical reports have described gastrointestinal symptoms. This is particularly true in children in whom gastrointestinal symptoms are frequent and viral shedding outlasts viral clearance from the respiratory system. These observations raise the question of whether the virus can replicate within the stomach. Here gastric organoids were generated from fetal, pediatric, and adult biopsies as in vitro models of SARS-CoV-2 infection. To facilitate infection, we induce reverse polarity in the gastric organoids. It was found that the pediatric and late fetal gastric organoids are susceptible to infection with SARS-CoV-2, while viral replication is significantly lower in undifferentiated organoids of early fetal and adult origin. It was demonstrated that adult gastric organoids are more susceptible to infection following differentiation. Transcriptomic analysis was performed to reveal a moderate innate antiviral response and a lack of differentially expressed genes belonging to the interferon family. Collectively, it was shown that the virus can efficiently infect the gastric epithelium, suggesting that the stomach might have an active role in fecal-oral SARS-CoV-2 transmission.

Reference

https://www.nature.com/articles/s41467-021-26762-2

An aluminum hydroxide: CpG adjuvant enhances protection elicited by a SARS-CoV-2 receptor-binding domain vaccine in aged mice

Abstract

Global deployment of vaccines that can provide protection across several age groups is still urgently needed to end the COVID-19 pandemic, especially in low- and middle-income countries. Although vaccines against SARS-CoV-2 based on mRNA and adenoviral-vector technologies have been rapidly developed, additional practical and scalable SARS-CoV-2 vaccines are required to meet global demand. Protein subunit vaccines formulated with appropriate adjuvants represent an approach to address this urgent need. The receptor-binding domain (RBD) is a key target of SARS-CoV-2 neutralizing antibodies but is poorly immunogenic. It was therefore compared that the pattern recognition receptor (PRR) agonists alone or formulated with aluminum hydroxide (AH) and benchmarked them against AS01B and AS03-like emulsion-based adjuvants for their potential to enhance RBD immunogenicity in young and aged mice. We found that an AH and CpG adjuvant formulation (AH:CpG) produced an 80-fold increase in anti-RBD neutralizing antibody titers in both age groups relative to AH alone and protected aged mice from the SARS-CoV-2 challenge. The AH:CpG-adjuvanted RBD vaccine elicited neutralizing antibodies against both wild-type SARS-CoV-2 and the B.1.351 (beta) variant at serum concentrations comparable to those induced by the licensed Pfizer-BioNTech BNT162b2 mRNA vaccine. AH:CpG induced similar cytokine and chemokine gene enrichment patterns in the draining lymph nodes of both young adult and aged mice and enhanced cytokine and chemokine production in human mononuclear cells of younger and older adults. These data support further development of AH:CpG-adjuvanted RBD as an affordable vaccine that may be effective across multiple age groups.

Reference

https://www.science.org/doi/10.1126/scitranslmed.abj5305

Neutralising antibody titres as predictors of protection against SARS-CoV-2 variants and the impact of boosting: A meta-analysis

Abstract

Background: Several SARS-CoV-2 variants of concern have been identified that partly escape serum neutralisation elicited by current vaccines. Studies have also shown that vaccines demonstrate reduced protection against symptomatic infection with SARS-CoV-2 variants. It was explored whether in-vitro neutralisation titres remain predictive of vaccine protection from infection with SARS-CoV-2 variants.

Methods: In this meta-analysis, published data was analysed from 24 identified studies on in-vitro neutralisation and clinical protection to understand the loss of neutralisation to existing SARS-CoV-2 variants of concern. The results of this analysis were integrated into our existing statistical model relating *in-vitro* neutralisation to protection (parameterised on data from ancestral virus infection) to estimate vaccine efficacy against SARS-CoV-2 variants. Data was also analyzed on boosting of vaccine responses and use the model to predict the impact of booster vaccination on protection against SARS-CoV-2 variants.

Findings: The neutralizing activity against the ancestral SARS-CoV-2 was highly predictive of neutralisation of variants of concern. Decreases in neutralisation titre to the alpha (1·6-fold), beta (8·8-fold), gamma (3·5-fold), and delta (3·9-fold) variants (compared to the ancestral virus) were not significantly different between different vaccines. Neutralisation remained strongly correlated with protection from symptomatic infection with SARS-CoV-2 variants of concern (rS=0·81, p=0·0005) and the existing model remained predictive of vaccine efficacy against variants of concern once decreases in neutralisation to the variants of concern were incorporated. Modelling of predicted vaccine efficacy against variants over time suggested that protection against symptomatic infection might decrease below 50% within the first year after vaccination for some vaccines. Boosting of previously infected individuals with existing vaccines (which target ancestral virus) is predicted to provide a higher degree of protection from infection with variants of concern than primary vaccination schedules alone.

Interpretation: *In-vitro* neutralisation titres remain a correlate of protection from SARS-CoV-2 variants and modelling of the effects of waning immunity predicts a loss of protection to the variants after vaccination. However, booster vaccination with current vaccines should enable higher neutralisation to SARS-CoV-2 variants than is achieved with primary vaccination, which is predicted to provide robust protection from severe infection outcomes with the current SARS-CoV-2 variants of concern, at least in the medium term.

Reference

https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247(21)00267-6/fulltext

Dexamethasone modulates immature neutrophils and interferon programming in severe COVID-19

Abstract

Although critical for host defense, innate immune cells are also pathologic drivers of acute respiratory distress syndrome (ARDS). Innate immune dynamics during Coronavirus Disease 2019 (COVID-19) ARDS, compared to ARDS from other respiratory pathogens, is unclear. Moreover, mechanisms underlying the beneficial effects of dexamethasone during severe COVID-19 remain elusive. Using single-cell RNA sequencing and plasma proteomics, it was discovered that, compared to bacterial ARDS, COVID-19 was associated with expansion of distinct neutrophil states characterized by interferon (IFN) and prostaglandin signaling. Dexamethasone during severe COVID-19 affected circulating neutrophils, altered IFNactive neutrophils, downregulated interferon-stimulated genes and activated IL-1R2+ neutrophils. Dexamethasone also expanded immunosuppressive immature neutrophils and remodeled cellular interactions by changing neutrophils from information receivers into information providers. Male patients had higher proportions of IFNactive neutrophils and preferential steroid-induced immature neutrophil expansion, potentially affecting outcomes. The single-cell atlas (see ‘Data availability’ section) defines COVID-19-enriched neutrophil states and molecular mechanisms of dexamethasone action to develop targeted immunotherapies for severe COVID-19.

Reference

https://www.nature.com/articles/s41591-021-01576-3

SARS-CoV-2 detection using reverse transcription strand invasion based amplification and a portable compact size instrument

Abstract

Rapid nucleic-acid based tests that can be performed by non-professionals outside laboratory settings could help the containment of the pandemic SARS-CoV-2 virus and may potentially prevent further widespread lockdowns. Here, a novel compact portable detection instrument (the Egoo Health System) was presented for extraction-free detection of SARS-CoV-2 using isothermal reverse transcription strand invasion based amplification (RT-SIBA). The SARS-CoV-2 RT-SIBA assay can be performed directly on crude oropharyngeal swabs without nucleic acid extraction with a reaction time of 30 min. The Egoo Health system uses a capsule system, which is automatically sealed tight in the Egoo instrument after applying the sample, resulting in a closed system optimal for molecular isothermal amplification. The performance of the Egoo Health System is comparable to the PCR instrument with an analytical sensitivity of 25 viral RNA copies per SARS-CoV-2 RT-SIBA reaction and a clinical sensitivity and specificity between 87.0–98.4% and 96.6–98.2% respectively.

Reference

https://www.nature.com/articles/s41598-021-01744-y

A case report describing the immune response of an infant with congenital heart disease and severe COVID-19

Abstract

Background: Children with SARS-CoV-2 infection generally present with milder symptoms or are asymptomatic in comparison with adults, however severe disease occurs in a subset of children. To date, the immune correlates of severe COVID-19 in young children have been poorly characterised.

Methods: The kinetics of immune responses were reported in relation to clinical and virological features in an infant with acute severe COVID-19 using high-dimensional flow cytometry and multiplex cytokine analysis.

Results: Systemic cellular and cytokine profiling show an initial increase in neutrophils and monocytes with depletion of lymphoid cell populations (particularly CD8 + T and NK cells) and elevated inflammatory cytokines. Expansion of memory CD4 + T (but not CD8 + T) cells occurred over time, with a predominant Th2 bias. Marked activation of T cell populations observed during the acute infection gradually resolved as the child recovered. Substantial in vitro activation of T-cell populations and robust cytokine production, in response to inactivated SARS-CoV-2 stimulation, was observed 3 months after infection indicating durable, long-lived cellular immune memory.

Conclusions: These findings provide important insights into the immune response of a young infant with severe COVID-19 and will help to inform future research into therapeutic targets for high-risk groups.

Reference

https://www.nature.com/articles/s43856-021-00047-7

The glycosylation in SARS-CoV-2 and its receptor ACE2

Abstract

Coronavirus disease 2019 (COVID-19), a highly infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has infected more than 235 million individuals and led to more than 4.8 million deaths worldwide as of October 5 2021. Cryo-electron microscopy and topology show that the SARS-CoV-2 genome encodes lots of highly glycosylated proteins, such as spike (S), envelope (E), membrane (M), and ORF3a proteins, which are responsible for host recognition, penetration, binding, recycling and pathogenesis. Here the detections, substrates, biological functions of the glycosylation in SARS-CoV-2 proteins as well as the human receptor ACE2 were reviewed, and also summarized the approved and undergoing SARS-CoV-2 therapeutics associated with glycosylation. This review may not only broad the understanding of viral glycobiology, but also provide key clues for the

development of new preventive and therapeutic methodologies against SARS-CoV-2 and its variants.

Reference

https://www.nature.com/articles/s41392-021-00809-8

SARS-CoV-2 inhibits induction of the MHC class I pathway by targeting the STAT1-IRF1-NLRC5 axis

Abstract

The MHC class I-mediated antigen presentation pathway plays a critical role in antiviral immunity. Here it was shown that the MHC class I pathway is targeted by SARS-CoV-2. Analysis of the gene expression profile from COVID-19 patients as well as SARS-CoV-2 infected epithelial cell lines reveals that the induction of the MHC class I pathway is inhibited by SARS-CoV-2 infection. It was shown that NLRC5, an MHC class I transactivator, is suppressed both transcriptionally and functionally by the SARS-CoV-2 ORF6 protein, providing a mechanistic link. SARS-CoV-2 ORF6 hampers type II interferon-mediated STAT1 signaling, resulting in diminished upregulation of NLRC5 and IRF1 gene expression. Moreover, SARS-CoV-2 ORF6 inhibits NLRC5 function *via* blocking karyopherin complex-dependent nuclear import of NLRC5. Collectively, the study uncovers an immune evasion mechanism of SARS-CoV-2 that targets the function of key MHC class I transcriptional regulators, STAT1-IRF1-NLRC5.

Reference

https://www.nature.com/articles/s41467-021-26910-8

Model-based estimation of transmissibility and reinfection of SARS-CoV-2 P.1 variant

Abstract

Background: The SARS-CoV-2 variant of concern (VOC) P.1 (Gamma variant) emerged in the Amazonas State, Brazil, in November 2020. The epidemiological consequences of its mutations have not been widely studied, despite detection of P.1 in 36 countries, with local transmission in at least 5 countries. A range of mutations are seen in P.1, ten

of them in the spike protein. It shares mutations with VOCs previously detected in the United Kingdom (B.1.1.7, Alpha variant) and South Africa (B.1.351, Beta variant).

Methods: The transmissibility and reinfection of P.1 were estimated using a model-based approach, fitting data from the national health surveillance of hospitalized individuals and frequency of the P.1 variant in Manaus from December-2020 to February-2021.

Results: Here it was estimated that the new variant is about 2.6 times more transmissible (95% Confidence Interval: 2.4–2.8) than previous circulating variant(s). Manaus already had a high prevalence of individuals previously affected by the SARS-CoV-2 virus and our fitted model attributed 28% of Manaus cases in the period to reinfections by P.1, confirming the importance of reinfection by this variant. This value is in line with estimates from blood donors samples in Manaus city.

Conclusions: P.1 was ranked as one of the most transmissible among the SARS-CoV-2 VOCs currently identified, and potentially as transmissible as the posteriorly detected VOC B.1.617.2 (Delta variant), posing a serious threat and requiring measures to control its global spread.

Reference

https://www.nature.com/articles/s43856-021-00048-6

Interaction of Spike protein and lipid membrane of SARS-CoV-2 with Ursodeoxycholic acid, an *in-silico* analysis

Abstract

Numerous repositioned drugs have been sought to decrease the severity of SARS-CoV-2 infection. It is known that among its physicochemical properties, Ursodeoxycholic Acid (UDCA) has a reduction in surface tension and cholesterol solubilization, it has also been used to treat cholesterol gallstones and viral hepatitis. In this study, molecular docking was performed with the SARS-CoV-2 Spike protein and UDCA. In order to confirm this interaction, Molecular Dynamics (MD) in “SARS-CoV-2 Spike protein-UDCA” were used. Using another system, it was also simulated MD with six UDCA residues around the Spike protein at random, naming this “SARS-CoV-2 Spike protein-6UDCA”. Finally, the possible interaction was evaluated between UDCA and different

types of membranes, considering the possible membrane conformation of SARS-CoV-2, this was named “SARS-CoV-2 membrane-UDCA”. In the “SARS-CoV-2 Spike protein-UDCA”, we found that UDCA exhibits affinity towards the central region of the Spike protein structure of − 386.35 kcal/mol, in a region with 3 alpha helices, which comprises residues from K986 to C1032 of each monomer. MD confirmed that UDCA remains attached and occasionally forms hydrogen bonds with residues R995 and T998. In the presence of UDCA, it was observed that the distances between residues atoms OG1 and CG2 of T998 in the monomers A, B, and C in the prefusion state do not change and remain at 5.93 ± 0.62 and 7.78 ± 0.51 Å, respectively, compared to the post-fusion state. Next, in “SARS-CoV-2 Spike protein-6UDCA”, the three UDCA showed affinity towards different regions of the Spike protein, but only one of them remained bound to the region between the region's heptad repeat 1 and heptad repeat 2 (HR1 and HR2) for 375 ps of the trajectory. The RMSD of monomer C was the smallest of the three monomers with a value of 2.89 ± 0.32, likewise, the smallest RMSF was also of the monomer C (2.25 ± 056). In addition, in the simulation of “SARS-CoV-2 membrane-UDCA”, UDCA had a higher affinity toward the virion-like membrane; where three of the four residues remained attached once they were close (5 Å, to the centre of mass) to the membrane by 30 ns. However, only one of them remained attached to the plasma-like membrane and this was in a cluster of cholesterol molecules. We have shown that UDCA interacts in two distinct regions of Spike protein sequences. In addition, UDCA tends to stay bound to the membrane, which could potentially reduce the internalization of SARS-CoV-2 in the host cell.

Reference

https://www.nature.com/articles/s41598-021-01705-5

SARS CoV-2 Delta variant exhibits enhanced infectivity and a minor decrease in neutralization sensitivity to convalescent or post-vaccination sera

Abstract

Since their identification, SARS-CoV-2 Kappa and Delta have rapidly spread to become globally dominant. However, their infectivity and sensitivity to administered vaccines have not been documented. Neutralization potential of convalescent or BNT162b2-post-vaccination sera against Kappa and Delta SARS-CoV-2 pseudoviruses was monitored.

It was shown that both variants were successfully neutralized by convalescent and post-vaccination sera, exhibiting a mild decrease in their neutralization sensitivity. Of the two variants, Delta presented enhanced infectivity levels compared to Kappa or wild-type SARS-CoV-2. Nevertheless, both variants were not as infectious or resistant to post-vaccination sera as the Beta variant of concern. Interestingly, the Delta plus variant (AY.1/B.1.617.2.1) exhibited high resistance to post-vaccination sera, similar to that of the Beta SARS-CoV-2. However, its infectivity levels were close to those of wild-type SARS-CoV2. These results account for the worldwide prevalence of Delta variant of concern, and confirm the efficacy of the BNT162b2-vaccine against circulating other Delta variants.

Reference

https://www.cell.com/iscience/fulltext/S2589-0042(21)01438-3

Publication Date: Nov 12, 2021

Burdens of post-acute sequelae of COVID-19 by severity of acute infection, demographics and health status

Abstract

The Post-Acute Sequelae of SARS-CoV-2 infection (PASC) have been characterized; however, the burden of PASC remains unknown. Here the healthcare databases of the US Department of Veterans Affairs were used to build a cohort of 181,384 people with COVID-19 and 4,397,509 non-infected controls and estimated that burden of PASC—defined as the presence of at least one sequela in excess of non-infected controls—was 73.43 (72.10, 74.72) per 1000 persons at 6 months. Burdens of individual sequelae varied by demographic groups (age, race, and sex) but were consistently higher in people with poorer baseline health and in those with more severe acute infection. In sum, the burden of PASC is substantial; PASC is non-monolithic with sequelae that are differentially expressed in various population groups. Collectively, the results may be useful in informing health systems capacity planning and care strategies of people with PASC.

Reference

https://www.nature.com/articles/s41467-021-26513-3

SARS-CoV-2 B.1.1.7 (alpha) and B.1.351 (beta) variants induce pathogenic patterns in K18-hACE2 transgenic mice distinct from early strains

Abstract

SARS-CoV-2 variants of concern (VOC) B.1.1.7 (alpha) and B.1.351 (beta) show increased transmissibility and enhanced antibody neutralization resistance. Here we demonstrate in K18-hACE2 transgenic mice that B.1.1.7 and B.1.351 are 100-fold more lethal than the original SARS-CoV-2 bearing 614D. B.1.1.7 and B.1.351 cause more severe organ lesions in K18-hACE2 mice than early SARS-CoV-2 strains bearing 614D or 614G, with B.1.1.7 and B.1.351 infection resulting in distinct tissue-specific cytokine signatures, significant D-dimer depositions in vital organs and less pulmonary hypoxia signaling before death. However, K18-hACE2 mice with prior infection of early SARS-CoV-2 strains or intramuscular immunization of viral spike or receptor binding domain are resistant to the lethal reinfection of B.1.1.7 or B.1.351, despite having reduced neutralization titers against these VOC than early strains. The results thus distinguish pathogenic patterns in K18-hACE2 mice caused by B.1.1.7 and B.1.351 infection from those induced by early SARS-CoV-2 strains, and help inform potential medical interventions for combating COVID-19.

Reference

https://www.nature.com/articles/s41467-021-26803-w

Bioengineered angiotensin-converting-enzyme-2: A potential therapeutic option against SARS-CoV-2 infection

Abstract

The recombinant soluble human angiotensin-converting enzyme 2 (rshACE2) is a promising therapy against SARS-CoV-2 infection, but it has some drawbacks that reduce the success of its clinical applications. The bioengineered ACE2 (Tag-sACE2 and probiotic-ACE2) as a way may overcome its therapeutic limitations against ongoing current pandemic.

Reference

https://www.nature.com/articles/s41371-021-00636-y

Common cardiac medications potently inhibit ACE2 binding to the SARS-CoV-2 Spike, and block virus penetration and infectivity in human lung cells

Abstract

To initiate SARS-CoV-2 infection, the Receptor Binding Domain (RBD) on the viral spike protein must first bind to the host receptor ACE2 protein on pulmonary and other ACE2-expressing cells. It was hypothesized that cardiac glycoside drugs might block the binding reaction between ACE2 and the Spike (S) protein, and thus block viral penetration into target cells. To test this hypothesis we developed a biochemical assay for ACE2:Spike binding, and tested cardiac glycosides as inhibitors of binding. Here it was reported that ouabain, digitoxin, and digoxin, as well as sugar-free derivatives digitoxigenin and digoxigenin, are high-affinity competitive inhibitors of ACE2 binding to the Original [D614] S1 and the α/β/γ [D614G] S1 proteins. These drugs also inhibit ACE2 binding to the Original RBD, as well as to RBD proteins containing the β [E484K], Mink [Y453F] and α/β/γ [N501Y] mutations. As hypothesized, we also found that ouabain, digitoxin and digoxin blocked penetration by SARS-CoV-2 Spike-pseudotyped virus into human lung cells, and infectivity by native SARS-CoV-2. These data indicate that cardiac glycosides may block viral penetration into the target cell by first inhibiting ACE2:RBD binding. Clinical concentrations of ouabain and digitoxin are relatively safe for short term use for subjects with normal hearts. It has therefore not escaped our attention that these common cardiac medications could be deployed worldwide as inexpensive repurposed drugs for anti-COVID-19 therapy.

Reference

https://www.nature.com/articles/s41598-021-01690-9

Computational redesign of Fab CC12.3 with substantially better predicted binding affinity to SARS-CoV-2 than human ACE2 receptor

Abstract

SARS-CoV-2 is responsible for COVID-19 pandemic, causing large numbers of cases and deaths. It initiates entry into human cells by binding to the peptidase domain of angiotensin-converting enzyme 2 (ACE2) receptor *via* its receptor binding domain of S1 subunit of spike protein (SARS-CoV-2-RBD). Employing neutralizing antibodies to

prevent binding between SARS-CoV-2-RBD and ACE2 is an effective COVID-19 therapeutic solution. Previous studies found that CC12.3 is a highly potent neutralizing antibody that was isolated from a SARS-CoV-2 infected patient, and its Fab fragment (Fab CC12.3) bound to SARS-CoV-2-RBD with comparable binding affinity to ACE2. To enhance its binding affinity, we employed computational protein design to redesign all CDRs of Fab CC12.3 and molecular dynamics (MD) to validate their predicted binding affinities by the MM-GBSA method. MD results show that the predicted binding affinities of the three best designed Fabs CC12.3 (CC12.3-D02, CC12.3-D05, and CC12.3-D08) are better than those of Fab CC12.3 and ACE2. Additionally, our results suggest that enhanced binding affinities of CC12.3-D02, CC12.3-D05, and CC12.3-D08 are caused by increased SARS-CoV-2-RBD binding interactions of CDRs L1 and L3. This study redesigned neutralizing antibodies with better predicted binding affinities to SARS-CoV-2-RBD than Fab CC12.3 and ACE2. They are promising candidates as neutralizing antibodies against SARS-CoV-2.

Reference

https://www.nature.com/articles/s41598-021-00684-x

Nucleocapsid mutations R203K/G204R increase the infectivity, fitness, and virulence of SARS-CoV-2

Abstract

Previous work found that the co-occurring mutations R203K/G204R on the SARS-CoV-2 nucleocapsid (N) protein are increasing in frequency among emerging variants of concern or interest. Through a combination of *in silico* analyses, this study demonstrates that R203K/G204R are adaptive, while large-scale phylogenetic analyses indicate that R203K/G204R associate with the emergence of the high-transmissibility SARS-CoV-2 lineage B.1.1.7. Competition experiments suggest that the 203K/204R variants possess a replication advantage over the preceding R203/G204 variants, possibly related to ribonucleocapsid (RNP) assembly. Moreover, the 203K/204R virus shows increased infectivity in human lung cells and hamsters. Accordingly, a positive association was observed between increased COVID-19 severity and sample frequency of 203K/204R. The work suggests that the 203K/204R mutations contribute to the increased transmission and virulence of select SARS-CoV-2 variants. In addition to

mutations in the spike protein, mutations in the nucleocapsid protein are important for viral spreading during the pandemic.

Reference

https://www.cell.com/cell-host-microbe/fulltext/S1931-3128(21)00511-4

Publication Date: Nov 11, 2021

Intravenous immunoglobulins in patients with COVID-19-associated moderate-to-severe acute respiratory distress syndrome (ICAR): Multicentre, double-blind, placebo-controlled, phase 3 trial

Abstract

Background: Acute respiratory distress syndrome (ARDS) is a major complication of COVID-19 and is associated with high mortality and morbidity. It was aimed to assess whether intravenous immunoglobulins (IVIG) could improve outcomes by reducing inflammation-mediated lung injury.

Methods: In this multicentre, double-blind, placebo-controlled trial, done at 43 centres in France, we randomly assigned patients (1:1) receiving invasive mechanical ventilation for up to 72 h with PCR confirmed COVID-19 and associated moderate-to-severe ARDS to receive either IVIG (2 g/kg over 4 days) or placebo. Random assignment was done with a web-based system and was stratified according to the participating centre and the duration of invasive mechanical ventilation before inclusion in the trial (<12 h, 12–24 h, and >24–72 h), and treatment was administered within the first 96 h of invasive mechanical ventilation. To minimise the risk of adverse events, the IVIG administration was divided into four perfusions of 0·5 g/kg each administered over at least 8 hours. Patients in the placebo group received an equivalent volume of sodium chloride 0·9% (10 mL/kg) over the same period. The primary outcome was the number of ventilation-free days by day 28, assessed according to the intention-to-treat principle. This trial was registered on ClinicalTrials.gov, NCT04350580.

Findings: Between April 3, and October 20, 2020, 146 patients (43 [29%] women) were eligible for inclusion and randomly assigned: 69 (47%) patients to the IVIG group and 77 (53%) to the placebo group. The intention-to-treat analysis showed no statistical difference in the median number of ventilation-free days at day 28 between the IVIG

group (0·0 [IQR 0·0–8·0]) and the placebo group (0·0 [0·0–6·0]; difference estimate 0·0 [0·0–0·0]; p=0·21). Serious adverse events were more frequent in the IVIG group (78 events in 22 [32%] patients) than in the placebo group (47 events in 15 [20%] patients; p=0·089).

Interpretation: In patients with COVID-19 who received invasive mechanical ventilation for moderate-to-severe ARDS, IVIG did not improve clinical outcomes at day 28 and tended to be associated with an increased frequency of serious adverse events, although not significant. The effect of IVIGs on earlier disease stages of COVID-19 should be assessed in future trials.

Reference

https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00440-9/fulltext

Safety and immunogenicity of concomitant administration of COVID-19 vaccines (ChAdOx1 or BNT162b2) with seasonal influenza vaccines in adults in the UK (ComFluCOV): A multicentre, randomised, controlled, phase 4 trial

Abstract

Background: Concomitant administration of COVID-19 and influenza vaccines could reduce burden on health-care systems. It was aimed to assess the safety of concomitant administration of ChAdOx1 or BNT162b2 plus an age-appropriate influenza vaccine.

Methods: In this multicentre, randomised, controlled, phase 4 trial, adults in receipt of a single dose of ChAdOx1 or BNT162b2 were enrolled at 12 UK sites and randomly assigned (1:1) to receive concomitant administration of either an age-appropriate influenza vaccine or placebo alongside their second dose of COVID-19 vaccine. 3 weeks later the group who received placebo received the influenza vaccine, and vice versa. Participants were followed up for 6 weeks. The influenza vaccines were three seasonal, inactivated vaccines (trivalent, MF59C adjuvanted or a cellular or recombinant quadrivalent vaccine). Participants and investigators were masked to the allocation. The primary endpoint was one or more participant-reported solicited systemic reactions in the 7 days after first trial vaccination(s), with a difference of less than 25% considered non-inferior. Analyses were done on an intention-to-treat basis. Local and

unsolicited systemic reactions and humoral responses were also assessed. The trial is registered with ISRCTN, ISRCTN14391248.

Findings: Between April 1 and June 26, 2021, 679 participants were recruited to one of six cohorts, as follows: 129 ChAdOx1 plus cellular quadrivalent influenza vaccine, 139 BNT162b2 plus cellular quadrivalent influenza vaccine, 146 ChAdOx1 plus MF59C adjuvanted, trivalent influenza vaccine, 79 BNT162b2 plus MF59C adjuvanted, trivalent influenza vaccine, 128 ChAdOx1 plus recombinant quadrivalent influenza vaccine, and 58 BNT162b2 plus recombinant quadrivalent influenza vaccine. 340 Participants were assigned to concomitant administration of influenza and a second dose of COVID-19 vaccine at day 0 followed by placebo at day 21, and 339 participants were randomly assigned to concomitant administration of placebo and a second dose of COVID-19 vaccine at day 0 followed by influenza vaccine at day 21. Non-inferiority was indicated in four cohorts, as follows: ChAdOx1 plus cellular quadrivalent influenza vaccine (risk difference for influenza vaccine minus placebos −1·29%, 95% CI −14·7 to 12·1), BNT162b2 plus cellular quadrivalent influenza vaccine (6·17%, −6·27 to 18·6), BNT162b2 plus MF59C adjuvanted, trivalent influenza vaccine (–12·9%, −34·2 to 8·37), and ChAdOx1 plus recombinant quadrivalent influenza vaccine (2·53%, −13·3 to 18·3). In the other two cohorts, the upper limit of the 95% CI exceeded the 0·25 non-inferiority margin (ChAdOx1 plus MF59C adjuvanted, trivalent influenza vaccine 10·3%, −5·44 to 26·0; BNT162b2 plus recombinant quadrivalent influenza vaccine 6·75%, −11·8 to 25·3). Most systemic reactions to vaccination were mild or moderate. Rates of local and unsolicited systemic reactions were similar between the randomly assigned groups. One serious adverse event, hospitalisation with severe headache, was considered related to the trial intervention. Immune responses were not adversely affected.

Interpretation: Concomitant vaccination with ChAdOx1 or BNT162b2 plus an age-appropriate influenza vaccine raises no safety concerns and preserves antibody responses to both vaccines. Concomitant vaccination with both COVID-19 and influenza vaccines over the next immunization season should reduce the burden on health-care services for vaccine delivery, allowing for timely vaccine administration and protection from COVID-19 and influenza for those in need.

Reference

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)02329-1/fulltext

Efficacy, safety, and lot-to-lot immunogenicity of an inactivated SARS-CoV-2 vaccine (BBV152): Interim results of a randomised, double-blind, controlled, phase 3 trial

Abstract

Background: It was reported the clinical efficacy against COVID-19 infection of BBV152, a whole virion inactivated SARS-CoV-2 vaccine formulated with a toll-like receptor 7/8 agonist molecule adsorbed to alum (Algel-IMDG) in Indian adults.

Methods: A randomised, double-blind, placebo-controlled, multicentre, phase 3 clinical trial was done in 25 Indian hospitals or medical clinics to evaluate the efficacy, safety, and immunological lot consistency of BBV152. Adults (age ≥18 years) who were healthy or had stable chronic medical conditions (not an immunocompromising condition or requiring treatment with immunosuppressive therapy) were randomised 1:1 with a computer-generated randomisation scheme (stratified for the presence or absence of chronic conditions) to receive two intramuscular doses of vaccine or placebo administered 4 weeks apart. Participants, investigators, study coordinators, study-related personnel, the sponsor, and nurses who administered the vaccines were masked to treatment group allocation; an unmasked contract research organisation and a masked expert adjudication panel assessed outcomes. The primary outcome was the efficacy of the BBV152 vaccine in preventing a first occurrence of laboratory-confirmed (RT-PCR-positive) symptomatic COVID-19 (any severity), occurring at least 14 days after the second dose in the per-protocol population. Safety and reactogenicity were also assessed throughout the duration of the study in all participants who had received at least one dose of vaccine or placebo. This report contains interim results (data cutoff May 17, 2021) regarding immunogenicity and safety outcomes (captured on days 0 to 56) and efficacy results with a median of 99 days for the study population. The trial was registered on the Indian Clinical Trials Registry India, CTRI/2020/11/028976, and ClinicalTrials.gov, NCT04641481 (active, not recruiting).

Findings: Between Nov 16, 2020, and Jan 7, 2021, 25 798 participants were recruited who were randomly assigned to receive BBV152 or placebo; 24 419 received two doses

of BBV152 (n=12 221) or placebo (n=12 198). Efficacy analysis was dependent on having 130 cases of symptomatic COVID-19, which occurred when 16 973 initially seronegative participants had at least 14 days follow-up after the second dose. 24 (0·3%) cases occurred among 8471 vaccine recipients and 106 (1·2%) among 8502 placebo recipients, giving an overall estimated vaccine efficacy of 77·8% (95% CI 65·2–86·4). In the safety population (n=25 753), 5959 adverse events occurred in 3194 participants. BBV152 was well tolerated; the same proportion of participants reported adverse events in the vaccine group (1597 [12·4%] of 12 879) and placebo group (1597 [12·4%] of 12 874), with no clinically significant differences in the distributions of solicited, unsolicited, or serious adverse events between the groups, and no cases of anaphylaxis or vaccine-related deaths.

Interpretation: BBV152 was highly efficacious against laboratory-confirmed symptomatic COVID-19 disease in adults. Vaccination was well tolerated with no safety concerns raised in this interim analysis.

Reference

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)02000-6/fulltext

Exposing structural variations in SARS-CoV-2 evolution

Abstract

The mutation of SARS-CoV-2 influences viral function as residue replacements affect both physiochemical properties and folding conformations. Although a large amount of data on SARS-CoV-2 is available, the investigation of how viral functions change in response to mutations is hampered by a lack of effective structural analysis. Here, we exploit the advances of protein structure fingerprint technology to study the folding conformational changes induced by mutations. With integration of both protein sequences and folding conformations, the structures are aligned for SARS-CoV to SARS-CoV-2, including Alpha variant (lineage B.1.1.7) and Delta variant (lineage B.1.617.2). The results showed that the virus evolution with change in mutational positions and physicochemical properties increased the affinity between spike protein and ACE2, which plays a critical role in coronavirus entry into human cells. Additionally, these structural variations impact vaccine effectiveness and drug function over the course of SARS-CoV-2 evolution. The analysis of structural variations revealed how the

coronavirus has gradually evolved in both structure and function and how the SARS-CoV-2 variants have contributed to more severe acute disease worldwide.

Reference

https://www.nature.com/articles/s41598-021-01650-3

A rapid simple point-of-care assay for the detection of SARS-CoV-2 neutralizing antibodies

Abstract

Background: Neutralizing antibodies (NAbs) prevent pathogens from infecting host cells. Detection of SARS-CoV-2 NAbs is critical to evaluate herd immunity and monitor vaccine efficacy against SARS-CoV-2, the virus that causes COVID-19. All currently available NAb tests are lab-based and time-intensive.

Method: A10 min cellulose pull-down test was developed to detect NAbs against SARS-CoV-2 from human plasma. The test evaluates the ability of antibodies to disrupt ACE2 receptor—RBD complex formation. The simple, portable, and rapid testing process relies on two key technologies: (i) the vertical-flow paper-based assay format and (ii) the rapid interaction of cellulose binding domain to cellulose paper.

Results: Here the construction of a cellulose-based vertical-flow test was shown. The developed test gives above 80% sensitivity and specificity and up to 93% accuracy as compared to two current lab-based methods using COVID-19 convalescent plasma.

Conclusions: A rapid 10 min cellulose based test has been developed for detection of NAb against SARS-CoV-2. The test demonstrates comparable performance to the lab-based tests and can be used at Point-of-Care. Importantly, the approach used for this test can be easily extended to test RBD variants or to evaluate NAbs against other pathogens.

Reference

https://www.nature.com/articles/s43856-021-00045-9

Direct comparison of antibody responses to four SARS-CoV-2 vaccines in Mongolia

Abstract

Different SARS-CoV-2 vaccines are approved in various countries, but few direct comparisons of the antibody responses they stimulate have been reported. We collected plasma specimens in July 2021 from 196 Mongolian participants fully vaccinated with one of four COVID-19 vaccines: Pfizer/BioNTech, AstraZeneca, Sputnik V and Sinopharm. Functional antibody testing with a panel of nine SARS-CoV-2 viral variant receptor binding domain (RBD) proteins reveal marked differences in vaccine responses, with low antibody levels and RBD-ACE2 blocking activity stimulated by the Sinopharm and Sputnik V vaccines in comparison to the AstraZeneca or Pfizer/BioNTech vaccines. The Alpha variant caused 97% of infections in Mongolia in June and early July 2021. Individuals who recover from SARS-CoV-2 infection after vaccination achieve high antibody titers in most cases. These data suggest that public health interventions such as vaccine boosting, potentially with more potent vaccine types, may be needed to control COVID-19 in Mongolia and worldwide.

Reference

https://www.cell.com/cell-host-microbe/fulltext/S1931-3128(21)00510-2