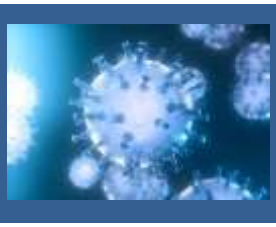
COVID-19

Sep 30 – Oct 06, 2021



RESEARCH PUBLICATIONS

Publication Date: Oct 05, 2021

Increased lethality in influenza and SARS-CoV-2 coinfection is prevented by influenza immunity but not SARS-CoV-2 immunity

Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the cause of the ongoing coronavirus disease 2019 (COVID-19) pandemic. The continued spread of SARS-CoV-2 increases the probability of influenza/SARS-CoV-2 coinfection, which may result in severe disease. In this study, we examine the disease outcome of influenza A virus (IAV) and SARS-CoV-2 coinfection in K18-hACE2 mice. Our data indicate enhance susceptibility of IAV-infected mice to developing severe disease upon coinfection with SARS-CoV-2 two days later. In contrast to nonfatal influenza and lower mortality rates due to SARS-CoV-2 alone, this coinfection results in severe morbidity and nearly complete mortality. Coinfection is associated with elevated influenza viral loads in respiratory organs. Remarkably, prior immunity to influenza, but not to SARS-CoV-2, prevents severe disease and mortality. This protection is antibody-dependent. These data experimentally support the necessity of seasonal influenza vaccination for reducing the risk of severe influenza/COVID-19 comorbidity during the COVID-19 pandemic.

Reference

https://www.nature.com/articles/s41467-021-26113-1

Expression and characterization of SARS-CoV-2 spike proteins

Abstract

The severe acute respiratory syndrome coronavirus 2 spike protein is a critical component of coronavirus disease 2019 vaccines and diagnostics and is also a therapeutic target. However, the spike protein is difficult to produce recombinantly because it is a large trimeric class I fusion membrane protein that is metastable and heavily glycosylated. We recently developed a prefusion-stabilized spike variant, termed HexaPro for six stabilizing proline substitutions, that can be expressed with a yield of >30 mg/L in ExpiCHO cells. This protocol describes an optimized workflow for expressing and biophysically characterizing rationally engineered spike proteins in Freestyle 293 and ExpiCHO cell lines. Although we focus on HexaPro, this protocol has been used to purify over a hundred different spike variants in our laboratories. We also provide guidance on expression quality control, long-term storage, and uses in enzyme-linked immunosorbent assays. The entire protocol, from transfection to biophysical characterization, can be completed in 7 d by researchers with basic tissue cell culture and protein purification expertise.

Reference

https://www.nature.com/articles/s41596-021-00623-0

Characterization of humoral and SARS-CoV-2 specific T cell responses in people living with HIV

Abstract

There is an urgent need to understand the nature of immune responses against SARS-CoV-2, to inform risk-mitigation strategies for people living with HIV (PLWH). Here we show that the majority of PLWH with ART suppressed HIV viral load, mount a detectable adaptive immune response to SARS-CoV-2. Humoral and SARS-CoV-2-specific T cell responses are comparable between HIV-positive and negative subjects and persist 5-7 months following predominately mild COVID-19 disease. T cell responses against Spike, Membrane and Nucleoprotein are the most prominent, with SARS-CoV-2-specific CD4 T cells outnumbering CD8 T cells. We further show that the overall magnitude of SARS-CoV-2-specific T cell responses relates to the size of the

naive CD4 T cell pool and the CD4:CD8 ratio in PLWH. These findings suggest that inadequate immune reconstitution on ART, could hinder immune responses to SARS-CoV-2 with implications for the individual management and vaccine effectiveness in PLWH.

Reference

https://www.nature.com/articles/s41467-021-26137-7

Mechanisms of SARS-CoV-2 entry into cells

Abstract

The unprecedented public health and economic impact of the COVID-19 pandemic caused by infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been met with an equally unprecedented scientific response. Much of this response has focused, appropriately, on the mechanisms of SARS-CoV-2 entry into host cells, and in particular the binding of the spike (S) protein to its receptor, angiotensin-converting enzyme 2 (ACE2), and subsequent membrane fusion. This Review provides the structural and cellular foundations for understanding the multistep SARS-CoV-2 entry process, including S protein synthesis, S protein structure, conformational transitions necessary for association of the S protein with ACE2, engagement of the receptor-binding domain of the S protein with ACE2, proteolytic activation of the S protein, endocytosis and membrane fusion. We define the roles of furin-like proteases, transmembrane protease, serine 2 (TMPRSS2) and cathepsin L in these processes, and delineate the features of ACE2 orthologues in reservoir animal species and S protein adaptations that facilitate efficient human transmission. We also examine the utility of vaccines, antibodies and other potential therapeutics targeting SARS-CoV-2 entry mechanisms. Finally, we present key outstanding questions associated with this critical process.

Reference

https://www.nature.com/articles/s41580-021-00418-x

Change sign detection with differential MDL change statistics and its applications to COVID-19 pandemic analysis

Abstract

We are concerned with the issue of detecting changes and their signs from a data stream. For example, when given time series of COVID-19 cases in a region, we may raise early warning signals of an epidemic by detecting signs of changes in the data. We propose a novel methodology to address this issue. The key idea is to employ a new information-theoretic notion, which we call the differential minimum description length change statistics (D-MDL), for measuring the scores of change sign. We first give a fundamental theory for D-MDL. We then demonstrate its effectiveness using synthetic datasets. We apply it to detecting early warning signals of the COVID-19 epidemic using time series of the cases for individual countries. We empirically demonstrate that D-MDL is able to raise early warning signals of events such as significant increase/decrease of cases. Remarkably, for about \(64\%\) of the events of significant increase of cases in studied countries, our method can detect warning signals as early as nearly six days on average before the events, buying considerably long time for making responses. We further relate the warning signals to the dynamics of the basic reproduction number R0 and the timing of social distancing. The results show that our method is a promising approach to the epidemic analysis from a data science viewpoint.

Reference

https://www.nature.com/articles/s41598-021-98781-4

SARS-CoV-2 immune repertoire in MIS-C and pediatric COVID-19

Abstract

There is limited understanding of the viral antibody fingerprint following severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in children. Herein, SARS-CoV-2 proteome-wide immunoprofiling of children with mild/moderate or severe coronavirus disease 2019 (COVID-19) versus multisystem inflammatory syndrome in children versus hospitalized control patients revealed differential cytokine responses, IgM/IgG/IgA epitope diversity, antibody binding and avidity. Apart from spike and nucleocapsid, IgG/IgA recognized epitopes in nonstructural protein (NSP) 2, NSP3,

NSP12–NSP14 and open reading frame (ORF) 3a–ORF9. Peptides representing epitopes in NSP12, ORF3a and ORF8 demonstrated SARS-CoV-2 serodiagnosis. Antibody-binding kinetics with 24 SARS-CoV-2 proteins revealed antibody parameters that distinguish children with mild/moderate versus severe COVID-19 or multisystem inflammatory syndrome in children. Antibody avidity to prefusion spike correlated with decreased illness severity and served as a clinical disease indicator. The fusion peptide and heptad repeat 2 region induced SARS-CoV-2-neutralizing antibodies in rabbits. Thus, we identified SARS-CoV-2 antibody signatures in children associated with disease severity and delineate promising serodiagnostic and virus neutralization targets. These findings might guide the design of serodiagnostic assays, prognostic algorithms, therapeutics and vaccines in this important but understudied population.

Reference

https://www.nature.com/articles/s41590-021-01051-8

Genetic and phenotypic analysis of the causal relationship between aging and COVID-19

Abstract

Background: Epidemiological studies revealed that the elderly and those with comorbidities are most affected by COVID-19, but it is important to investigate shared genetic mechanisms between COVID-19 risk and aging.

Methods: A multi-instrument Mendelian Randomization analysis of multiple lifespan-related traits and COVID-19 was conducted. Aging clock models were applied to the subjects with different COVID-19 conditions in the UK-Biobank cohort. We performed a bivariate genomic scan for age-related COVID-19 and Mendelian Randomization analysis of 389 immune cell traits to investigate their effect on lifespan and COVID-19 risk.

Results: It was shown that the genetic variation that supports longer life is significantly associated with the lower risk of COVID-19 infection and hospitalization. The odds ratio is 0.31 ($P = 9.7 \times 10{-}6$) and 0.46 ($P = 3.3 \times 10{-}4$), respectively, per additional 10 years of life. We detect an association between biological age acceleration and future incidence and severity of COVID-19 infection. Genetic profiling of age-related COVID-

19 infection indicates key contributions of Notch signaling and immune system development. We reveal a negative correlation between the effects of immune cell traits on lifespan and COVID-19 risk. We find that lower B-cell CD19 levels are indicative of an increased risk of COVID-19 and decreased life expectancy, which is further validated by COVID-19 clinical data.

Conclusions: Our analysis suggests that the factors that accelerate aging lead to an increased COVID-19 risk and point to the importance of Notch signaling and B cells in both. Interventions that target these factors to reduce biological age may reduce the risk of COVID-19.

Reference

https://www.nature.com/articles/s43856-021-00033-z

Immunogenic T cell epitopes of SARS-CoV-2 are recognized by circulating memory and naïve CD8 T cells of unexposed individuals

Abstract

Background: Recent studies have provided evidence of T cell reactivity to Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in significant numbers of non-infected individuals, which has been attributed to cross-reactive CD4 memory T cells from previous exposure to seasonal coronaviruses. Less evidence of cross-reactive memory CD8 T cells has been documented to date.

Methods: The NetCTLPan neural network of the Epitope Database and Analysis Resource was used to select a series of 27 HLA-A*02:01 epitopes derived from the proteome of SARS-CoV-2. Their binding capacity was assessed by a HLA-A*02:01 stabilization assay and by quantifying their binding to HLA-A*02:01 monomers for the generation of tetramers. Their ability to stimulate and induce expansion of SARS-CoV-2 reactive CD8 T cells was measured by flow cytometry. The TCR repertoire of COVID convalescent and healthy unexposed donors was analysed using the MIRA database.

Findings: The HLA-A*02:01 epitopes tested were able to stabilise HLA molecules and induce activation of CD8 T cells of healthy unexposed donors. These results, based on specific tetramer binding, provide evidence supporting the presence of frequent cross-

reactive CD8 T cells to SARS-CoV-2 antigens in non-exposed individuals. Interestingly, the reactive cells were distributed into naïve, memory and effector subsets.

Interpretation: Our data are consistent with a significant proportion of the reactive CD8 T clones belonging to the public shared repertoire, readily available in absence of previous contact with closely related coronaviruses. Furthermore, we demonstrate the immunogenic capacity of long peptides carrying T cell epitopes, which can serve to isolate virus-specific T cell receptors among the ample repertoire of healthy unexposed subjects and could have application in COVID-19 immunotherapy. Limitations of our study are that it concentrated on one MHC I allele (HLA-A*02:01) and the low numbers of samples and epitopes tested.

Reference

https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(21)00403-5/fulltext

Publication Date: Oct 04, 2021

Detection and analysis of COVID-19 in medical images using deep learning techniques

Abstract

The main purpose of this work is to investigate and compare several deep learning enhanced techniques applied to X-ray and CT-scan medical images for the detection of COVID-19. In this paper, we used four powerful pre-trained CNN models, VGG16, DenseNet121, ResNet50,and ResNet152, for the COVID-19 CT-scan binary classification task. The proposed Fast.AI ResNet framework was designed to find out the best architecture, pre-processing, and training parameters for the models largely automatically. The accuracy and F1-score were both above 96% in the diagnosis of COVID-19 using CT-scan images. In addition, we applied transfer learning techniques to overcome the insufficient data and to improve the training time. The binary and multi-class classification of X-ray images tasks were performed by utilizing enhanced VGG16 deep transfer learning architecture. High accuracy of 99% was achieved by enhanced VGG16 in the detection of X-ray images from COVID-19 and pneumonia. The accuracy and validity of the algorithms were assessed on X-ray and CT-scan well-known public datasets. The proposed methods have better results for COVID-19 diagnosis than other

related in literature. In opinion, this work can help virologists and radiologists to make a better and faster diagnosis in the struggle against the outbreak of COVID-19.

Reference

https://www.nature.com/articles/s41598-021-99015-3

The SARS-CoV-2 first wave impact in the acute inflammatory surgical pathologies

Abstract

Anecdotal evidence suggests that community infection control measures during the COVID-19 outbreak have modified the number and natural history of acute surgical inflammatory processes (ASIP—appendicitis, cholecystitis, diverticulitis and perianal abscesses) admissions. This study aims to evaluate the impact of the COVID-19 pandemic on the presentation and treatment ASIP and quantify the effect of COVID-19 infection on the outcomes of ASIP patients. This was a multicentre, comparative study, whereby ASIP cases from 2019, 2020 and 2021 (March 14th to May 2nd) were analyzed. Data regarding patient and disease characteristics as well as outcomes, were collected from sixteen centres in Madrid, and one in Seville (Spain). The number of patients treated for ASIP in 2019 was 822 compared to 521 in 2020 and 835 in 2021. This 1/3rd reduction occurs mainly in patients with mild cases, while the number of severe cases was similar. Surgical standards suffered a step back during the first wave: Lower laparoscopic approach and longer length of stay. We also found a more conservative approach to the patients this year, non-justified by clinical circumstances. Luckily these standards improved again in 2021. The positive COVID-19 status itself did not have a direct impact on mortality. Strikingly, none of the 33 surgically treated COVID positive patients during both years died postoperatively. This is an interesting finding which, if confirmed through future research with a larger sample size of COVID-19 positive patients, can expedite the recovery phase of acute surgical services.

Reference

https://www.nature.com/articles/s41598-021-98878-w

Hamster organotypic modeling of SARS-CoV-2 lung and brainstem infection

Abstract

SARS-CoV-2 has caused a global pandemic of COVID-19 since its emergence in December 2019. The infection causes a severe acute respiratory syndrome and may also spread to central nervous system leading to neurological sequelae. We have developed and characterized two new organotypic cultures from hamster brainstem and lung tissues that offer a unique opportunity to study the early steps of viral infection and screening antivirals. These models are not dedicated to investigate how the virus reaches the brain. However, they allow validating the early tropism of the virus in the lungs and demonstrating that SARS-CoV-2 could infect the brainstem and the cerebellum, mainly by targeting granular neurons. Viral infection induces specific interferon and innate immune responses with patterns specific to each organ, along with cell death by apoptosis, necroptosis, and pyroptosis. Overall, our data illustrate the potential of rapid modeling of complex tissue-level interactions during infection by a newly emerged virus.

Reference

https://www.nature.com/articles/s41467-021-26096-z

COVID-19 and metabolic disease: Mechanisms and clinical management

Abstract

Up to 50% of the people who have died from COVID-19 had metabolic and vascular disorders. Notably, there are many direct links between COVID-19 and the metabolic and endocrine systems. Thus, not only are patients with metabolic dysfunction (eg, obesity, hypertension, non-alcoholic fatty liver disease, and diabetes) at an increased risk of developing severe COVID-19 but also infection with SARS-CoV-2 might lead to new-onset diabetes or aggravation of pre-existing metabolic disorders. In this Review, we provide an update on the mechanisms of how metabolic and endocrine disorders might predispose patients to develop severe COVID-19. Additionally, we update the practical recommendations and management of patients with COVID-19 and post-pandemic. Furthermore, we summarise new treatment options for patients with both COVID-19 and diabetes, and highlight current challenges in clinical management.

Reference

https://www.thelancet.com/journals/landia/article/PIIS2213-8587(21)00244-8/fulltext

Effectiveness of mRNA BNT162b2 COVID-19 vaccine up to 6 months in a large integrated health system in the USA: A retrospective cohort study

Abstract

Background: Vaccine effectiveness studies have not differentiated the effect of the delta (B.1.617.2) variant and potential waning immunity in observed reductions in effectiveness against SARS-CoV-2 infections. We aimed to evaluate overall and variant-specific effectiveness of BNT162b2 (tozinameran, Pfizer–BioNTech) against SARS-CoV-2 infections and COVID-19-related hospital admissions by time since vaccination among members of a large US health-care system.

Methods: In this retrospective cohort study, we analysed electronic health records of individuals (≥12 years) who were members of the health-care organisation Kaiser Permanente Southern California (CA, USA), to assess BNT162b2 vaccine effectiveness against SARS-CoV-2 infections and COVID-19-related hospital admissions for up to 6 months. Participants were required to have 1 year or more previous membership of the organisation. Outcomes comprised SARS-CoV-2 PCR-positive tests and COVID-19-related hospital admissions. Effectiveness calculations were based on hazard ratios from adjusted Cox models. This study was registered with ClinicalTrials.gov, NCT04848584.

Findings: Between Dec 14, 2020, and Aug 8, 2021, of 4 920 549 individuals assessed for eligibility, we included 3 436 957 (median age 45 years [IQR 29–61]; 1 799 395 [52·4%] female and 1 637 394 [47·6%] male). For fully vaccinated individuals, effectiveness against SARS-CoV-2 infections was 73% (95% CI 72–74) and against COVID-19-related hospital admissions was 90% (89–92). Effectiveness against infections declined from 88% (95% CI 86–89) during the first month after full vaccination to 47% (43–51) after 5 months. Among sequenced infections, vaccine effectiveness against infections of the delta variant was high during the first month after full vaccination (93% [95% CI 85–97]) but declined to 53% [39–65] after 4 months. Effectiveness against other (non-delta) variants the first month after full vaccination was also high at 97% (95% CI 95–99), but waned to 67% (45–80) at 4–5 months. Vaccine

effectiveness against hospital admissions for infections with the delta variant for all ages was high overall (93% [95% CI 84–96]) up to 6 months.

Interpretation: Our results provide support for high effectiveness of BNT162b2 against hospital admissions up until around 6 months after being fully vaccinated, even in the face of widespread dissemination of the delta variant. Reduction in vaccine effectiveness against SARS-CoV-2 infections over time is probably primarily due to waning immunity with time rather than the delta variant escaping vaccine protection.

Reference

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)02183-8/fulltext

Publication Date: Oct 01, 2021

Standardized preservation, extraction and quantification techniques for detection of fecal SARS-CoV-2 RNA

Abstract

Patients with COVID-19 shed SARS-CoV-2 RNA in stool, sometimes well after their respiratory infection has cleared. This may be significant for patient health, epidemiology, and diagnosis. However, methods to preserve stool, and to extract and quantify viral RNA are not standardized. We test the performance of three preservative approaches at yielding detectable SARS-CoV-2 RNA: the OMNIgene-GUT kit, Zymo DNA/RNA shield kit, and the most commonly applied, storage without preservative. We test these in combination with three extraction kits: QIAamp Viral RNA Mini Kit, Zymo Quick-RNA Viral Kit, and MagMAX Viral/Pathogen Kit. We also test the utility of ddPCR and RT-qPCR for the reliable quantification of SARS-CoV-2 RNA from stool. We identify that the Zymo DNA/RNA preservative and the QiaAMP extraction kit yield more detectable RNA than the others, using both ddPCR and RT-qPCR. Taken together, we recommend a comprehensive methodology for preservation, extraction and detection of RNA from SARS-CoV-2 and other coronaviruses in stool.

Reference

https://www.nature.com/articles/s41467-021-25576-6

Emergence and spread of SARS-CoV-2 lineage B.1.620 with variant of concern-like mutations and deletions

Abstract

Distinct SARS-CoV-2 lineages, discovered through various genomic surveillance initiatives, have emerged during the pandemic following unprecedented reductions in worldwide human mobility. We here describe a SARS-CoV-2 lineage - designated B.1.620 - discovered in Lithuania and carrying many mutations and deletions in the spike protein shared with widespread variants of concern (VOCs), including E484K, S477N and deletions HV69Δ, Y144Δ, and LLA241/243Δ. As well as documenting the suite of mutations this lineage carries, we also describe its potential to be resistant to neutralising antibodies, accompanying travel histories for a subset of European cases, evidence of local B.1.620 transmission in Europe with a focus on Lithuania, and significance of its prevalence in Central Africa owing to recent genome sequencing efforts there. We make a case for its likely Central African origin using advanced phylogeographic inference methodologies incorporating recorded travel histories of infected travellers.

Reference

https://www.nature.com/articles/s41467-021-26055-8

Publication Date: Sep 30, 2021

Feasibility of a surveillance programme based on gargle samples and pool testing to prevent SARS-CoV-2 outbreaks in schools

Abstract

School closures have a negative impact on physical and mental well-being, and education, of children and adolescents. A surveillance programme to detect asymptomatic SARS-CoV-2 infection could allow schools to remain open, while protecting the vulnerable. We assessed the feasibility of a programme employing gargle samples and pool testing of individually extracted RNA using rRT-qPCR in a primary and a secondary school in Germany, based on programme logistics and acceptance. Twice a week, five participants per class were selected to provide samples, using an algorithm weighted by a risk-based priority score to increase likelihood of case

detection. The positive response rate was 54.8% (550 of 1003 pupils). Logistics evaluation revealed the rate-limiting steps: completing the regular pre-test questionnaire and handing in the samples. Acceptance questionnaire responses indicated strong support for research into developing a surveillance programme and a positive evaluation of gargle tests. Participation was voluntary. As not all pupils participated, individual reminders could lead to participant identification. School-wide implementation of the programme for infection monitoring purposes would enable reminders to be given to all school pupils to address these steps, without compromising participant anonymity. Such a programme would provide a feasible means to monitor asymptomatic respiratory tract infection in schools.

Reference

https://www.nature.com/articles/s41598-021-98849-1

Quantitative modeling of the impact of facemasks and associated leakage on the airborne transmission of SARS-CoV-2

Abstract

The ongoing worldwide outbreak of COVID-19 has set personal protective equipment in the spotlight. A significant number of countries impose the use of facemasks in public spaces and encourage it in the private sphere. Even in countries where relatively high vaccination rates are achieved at present, breakthrough infections have been frequently reported and usage of facemasks in certain settings has been recommended again. Alternative solutions, including community masks fabricated using various materials, such as cotton or jersey, have emerged alongside facemasks following long-established standards (e.g., EN 149, EN 14683). In the present work, we present a computational model to calculate the ability of different types of facemasks to reduce the exposure to virus-laden respiratory particles, with a focus on the relative importance of the filtration properties and the fitting on the wearer's face. The model considers the facemask and the associated leakage, the transport of respiratory particles and their accumulation around the emitter, as well as the fraction of the inhaled particles deposited in the respiratory system. Different levels of leakages are considered to represent the diversity of fittings likely to be found among a population of non-trained users. The leakage prevails over the filtration performance of a facemask in determining the exposure level,

and the ability of a face protection to limit leakages needs to be taken into account to accurately estimate the provided protection. Filtering facepieces (FFP) provide a better protection efficiency than surgical and community masks due to their higher filtration efficiency and their ability to provide a better fit and thus reduce the leakages. However, an improperly-fitted FFP mask loses a critical fraction of its protection efficiency, which may drop below the protection level provided by properly-worn surgical and community masks.

Reference

https://www.nature.com/articles/s41598-021-98895-9

Theoretical and experimental study of interaction of macroheterocyclic compounds with ORF3a of SARS-CoV-2

Abstract

The pandemic infectious disease (Covid-19) caused by the coronavirus (SARS-CoV2) is spreading rapidly around the world. Covid-19 does an irreparable harm to the health and life of people. It also has a negative financial impact on the economies of most countries of the world. In this regard, the issue of creating drugs aimed at combating this disease is especially acute. In this work, molecular docking was used to study the docking of 23 compounds with QRF3a SARS-CoV2. The performed *in silico* modeling made it possible to identify leading compounds capable of exerting a potential inhibitory and virucidal effect. The leading compounds include chlorin (a drug used in PDT), iron(III)protoporphyrin (endogenous porphyrin), and tetraanthraquinone porphyrazine (an exogenous substance). Having taken into consideration the localization of ligands in the QRF3a SARS-CoV2, we have made an assumption about their influence on the pathogenesis of Covid-19. The interaction of chlorin, iron(III)protoporphyrin and protoporphyrin with the viral protein ORF3a were studied by fluorescence and UV–Vis spectroscopy. The obtained experimental results confirm the data of molecular docking. The results showed that a viral protein binds to endogenous porphyrins and chlorins, moreover, chlorin is a competitive ligand for endogenous porphyrins. Chlorin should be considered as a promising drug for repurposing.

Reference

https://www.nature.com/articles/s41598-021-99072-8

Mathematical modeling based on RT-qPCR analysis of SARS-CoV-2 in wastewater as a tool for epidemiology

Abstract

Coronavirus disease 2019 (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerges to scientific research and monitoring of wastewaters to predict the spread of the virus in the community. Our study investigated the COVID-19 disease in Bratislava, based on wastewater monitoring from September 2020 until March 2021. Samples were analyzed from two wastewater treatment plants of the city with reaching 0.6 million monitored inhabitants. Obtained results from the wastewater analysis suggest significant statistical dependence. High correlations between the number of viral particles in wastewater and the number of reported positive nasopharyngeal RT-qPCR tests of infected individuals with a time lag of 2 weeks/12 days ($R2 = 83.78\%/R2 = 52.65\%$) as well as with a reported number of death cases with a time lag of 4 weeks/27 days ($R2 = 83.21\%/R2 = 61.89\%$) was observed. The obtained results and subsequent mathematical modeling will serve in the future as an early warning system for the occurrence of a local site of infection and, at the same time, predict the load on the health system up to two weeks in advance.

Reference

https://www.nature.com/articles/s41598-021-98653-x

Possible future waves of SARS-CoV-2 infection generated by variants of concern with a range of characteristics

Abstract

Viral reproduction of SARS-CoV-2 provides opportunities for the acquisition of advantageous mutations, altering viral transmissibility, disease severity, and/or allowing escape from natural or vaccine-derived immunity. We use three mathematical models: a parsimonious deterministic model with homogeneous mixing; an age-structured model; and a stochastic importation model to investigate the effect of potential variants of concern (VOCs). Calibrating to the situation in England in May 2021, we find

epidemiological trajectories for putative VOCs are wide-ranging and dependent on their transmissibility, immune escape capability, and the introduction timing of a postulated VOC-targeted vaccine. We demonstrate that a VOC with a substantial transmission advantage over resident variants, or with immune escape properties, can generate a wave of infections and hospitalisations comparable to the winter 2020-2021 wave. Moreover, a variant that is less transmissible, but shows partial immune-escape could provoke a wave of infection that would not be revealed until control measures are further relaxed.

Reference

https://www.nature.com/articles/s41467-021-25915-7

Immune responses to two and three doses of the BNT162b2 mRNA vaccine in adults with solid tumors

Abstract

Vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have shown high efficacy, but immunocompromised participants were excluded from controlled clinical trials. In this study, we compared immune responses to the BNT162b2 mRNA Coronavirus Disease 2019 vaccine in patients with solid tumors (n = 53) who were on active cytotoxic anti-cancer therapy to a control cohort of participants without cancer (n = 50). Neutralizing antibodies were detected in 67% of patients with cancer after the first immunization, followed by a threefold increase in median titers after the second dose. Similar patterns were observed for spike protein-specific serum antibodies and T cells, but the magnitude of each of these responses was diminished relative to the control cohort. In most patients with cancer, we detected spike receptor-binding domain and other S1-specific memory B cell subsets as potential predictors of anamnestic responses to additional immunizations. We therefore initiated a phase 1 trial for 20 cancer cohort participants of a third vaccine dose of BNT162b2 (NCT04936997); primary outcomes were immune responses, with a secondary outcome of safety. At 1 week after a third immunization, 16 participants demonstrated a median threefold increase in neutralizing antibody responses, but no improvement was observed in T cell responses. Adverse events were mild. These results suggest that a

third dose of BNT162b2 is safe, improves humoral immunity against SARS-CoV-2 and could be immunologically beneficial for patients with cancer on active chemotherapy.

Reference

https://www.nature.com/articles/s41591-021-01542-z

Complementation of contact tracing by mass testing for successful containment of beta COVID-19 variant (SARS-CoV-2 VOC B.1.351) epidemic in Hong Kong

Abstract

Background: Global dissemination of SARS-CoV-2 Variants of Concern (VOCs) remains a concern. The aim of this study is to describe how mass testing and phylogenetic analysis successfully prevented local transmission of SARS-CoV-2 VOC in a densely populated city with low herd immunity for COVID-19.

Methods: In this descriptive study, we conducted contact tracing, quarantine, and mass testing of the potentially exposed contacts with the index case. Epidemiological investigation and phylogeographic analysis were performed.

Findings: Among 11,818 laboratory confirmed cases of COVID-19 diagnosed till 13th May 2021 in Hong Kong, SARS-CoV-2 VOCs were found in 271 (2.3%) cases. Except for 10 locally acquired secondary cases, all SARS-CoV-2 VOCs were imported or acquired in quarantine hotels. The index case of this SARS-CoV-2 VOC B.1.351 epidemic, an inbound traveler with asymptomatic infection, was diagnosed 9 days after completing 21 days of quarantine. Contact tracing of 163 contacts in household, hotel, and residential building only revealed 1 (0.6%) secondary case. A symptomatic foreign domestic helper (FDH) without apparent epidemiological link but infected by virus with identical genome sequence was subsequently confirmed. Mass testing of 0.34 million FDHs identified two more cases which were phylogenetically linked. A total of 10 secondary cases were identified that were related to two household gatherings. The clinical attack rate of household close contact was significantly higher than non-household exposure during quarantine (7/25, 28% vs 0/2051, 0%; $p<0.001$).

Interpretation: The rising epidemic of SARS-CoV-2 VOC transmission could be successfully controlled by contact tracing, quarantine, and rapid genome sequencing complemented by mass testing.

Reference

https://www.thelancet.com/journals/lanwpc/article/PIIS2666-6065(21)00190-5/fulltext

Early sample tagging and pooling enables simultaneous SARS-CoV-2 detection and variant sequencing

Abstract

Most severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) diagnostic tests have relied on RNA extraction followed by reverse transcription quantitative polymerase chain reaction (RT-qPCR) assays. Whereas automation improved logistics and different pooling strategies increased testing capacity, highly multiplexed next-generation sequencing (NGS) diagnostics remain a largely untapped resource. NGS tests have the potential to markedly increase throughput while providing crucial SARS-CoV-2 variant information. Current NGS-based detection and genotyping assays for SARS-CoV-2 are costly, mostly due to parallel sample processing through multiple steps. Here, we have established ApharSeq, in which samples are barcoded in the lysis buffer and pooled before reverse transcription. We validated this assay by applying ApharSeq to more than 500 clinical samples from the Clinical Virology Laboratory at Hadassah hospital in a robotic workflow. The assay was linear across five orders of magnitude, and the limit of detection was Ct 33 (~1000 copies/ml, 95% sensitivity) with >99.5% specificity. ApharSeq provided targeted high-confidence genotype information due to unique molecular identifiers incorporated into this method. Because of early pooling, we were able to estimate a 10- to 100-fold reduction in labor, automated liquid handling, and reagent requirements in high-throughput settings compared to current testing methods. The protocol can be tailored to assay other host or pathogen RNA targets simultaneously. These results suggest that ApharSeq can be a promising tool for current and future mass diagnostic challenges.

Reference

https://www.science.org/doi/10.1126/scitranslmed.abj2266

IN BRIEF

Publication Date: Oct 05, 2021

Cross-reactive tissue-resident CD8$^+$ T cells may provide first line of defence against SARS-CoV-2

Abstract

Cross-reactive CD4+ T cells, likely induced by common cold coronavirus infections, are detected in 20–50% of peripheral blood samples from SARS-CoV-2 unexposed individuals. However, cross-reactive CD8+ T cells are rarely detected in these samples. To study whether this may be because CD8+ memory T cells are mostly located in tissues, Niessl at al. examined peripheral blood and tonsillar tissue samples from pre-2019. Indeed, they detected SARS-CoV-2 reactive CD8+ memory T cells in 32% of tissue samples. Cross-reactive CD4+ cells were detected at similar levels in blood and tissue, whereas cross-reactive memory CD8+ T cells were largely absent in matched blood samples. Tissue-resident cross-reactive CD8+ memory T cells displayed markers of follicular homing and tissue residency, and the authors speculate that these may enable rapid sentinel immune responses to SARS-CoV-2.

Reference

https://www.nature.com/articles/s41577-021-00638-4