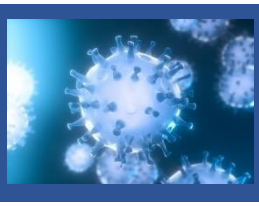
COVID-19

Oct 15 - 21, 2020



RESEARCH PUBLICATIONS

Publication Date: Oct 21, 2020

A pooled testing strategy for identifying SARS-CoV-2 at low prevalence

Abstract

Suppressing SARS-CoV-2 will likely require the rapid identification and isolation of infected individuals on an ongoing basis. Reverse transcription polymerase chain reaction (RT-PCR) tests are accurate but costly, making regular testing of every individual expensive. The costs are a challenge for all countries and particularly for developing countries. Cost reductions can be achieved by pooling (or combining) subsamples and testing them in groups1–7. A balance must be struck between increasing the group size and retaining test sensitivity, since sample dilution increases the likelihood of false negatives for individuals with low viral load in the sampled region at the time of the test8. Likewise, minimising the number of tests to reduce costs must be balanced against minimising the time testing takes to reduce the spread of infection. Here we propose an algorithm for pooling subsamples based on the geometry of a hypercube that, at low prevalence, accurately identifies infected individuals in a small number of tests and rounds of testing. We discuss the optimal group size and explain why, given the highly infectious nature of the disease, largely parallel searches are preferred. We report proof of concept experiments in which a positive subsample was detected even when diluted 100-fold with negative subsamples (cf. 30-fold to 48-fold dilution in Refs. 9–11). We quantify the loss of sensitivity due to dilution and discuss how it may be mitigated by frequent re-testing of groups, for example. With the use of these methods, the cost of mass testing could be reduced by a large factor which, furthermore, increases as the prevalence falls. Field trials of our approach are under way in Rwanda and South Africa. The use of group testing on a massive scale to closely and continually monitor infection in a population, along with rapid and effective

isolation of infected people, provides a promising pathway to the longterm control of COVID-19.

Reference

https://www.nature.com/articles/s41586-020-2885-5

Antibody-mediated disruption of the SARS-CoV-2 spike glycoprotein

Abstract

The CR3022 antibody, selected from a group of SARS-CoV monoclonal antibodies for its ability to cross-react with SARS-CoV-2, has been examined for its ability to bind to the ectodomain of the SARS-CoV-2 spike glycoprotein. Using cryo-electron microscopy we show that antibody binding requires rearrangements in the S1 domain that result in dissociation of the spike.

Reference

https://www.nature.com/articles/s41467-020-19146-5

Publication Date: Oct 20, 2020

A global survey of potential acceptance of a COVID-19 vaccine

Abstract

Several coronavirus disease 2019 (COVID-19) vaccines are currently in human trials. In June 2020, we surveyed 13,426 people in 19 countries to determine potential acceptance rates and factors influencing acceptance of a COVID-19 vaccine. Of these, 71.5% of participants reported that they would be very or somewhat likely to take a COVID-19 vaccine, and 61.4% reported that they would accept their employer's recommendation to do so. Differences in acceptance rates ranged from almost 90% (in China) to less than 55% (in Russia). Respondents reporting higher levels of trust in information from government sources were more likely to accept a vaccine and take their employer's advice to do so.

Reference

https://www.nature.com/articles/s41591-020-1124-9

The differential immune responses to COVID-19 in peripheral and lung revealed by single-cell RNA sequencing

Abstract

Understanding the mechanism that leads to immune dysfunction in severe coronavirus disease 2019 (COVID-19) is crucial for the development of effective treatment. Here, using single-cell RNA sequencing, we characterized the peripheral blood mononuclear cells (PBMCs) from uninfected controls and COVID-19 patients and cells in paired broncho-alveolar lavage fluid (BALF). We found a close association of decreased dendritic cells (DCs) and increased monocytes resembling myeloid-derived suppressor cells (MDSCs), which correlated with lymphopenia and inflammation in the blood of severe COVID-19 patients. Those MDSC-like monocytes were immune-paralyzed. In contrast, monocyte-macrophages in BALFs of COVID-19 patients produced massive amounts of cytokines and chemokines, but secreted little interferons. The frequencies of peripheral T cells and NK cells were significantly decreased in severe COVID-19 patients, especially for innate-like T and various CD8+ T cell subsets, compared to healthy controls. In contrast, the proportions of various activated CD4+ T cell subsets among the T cell compartment, including Th1, Th2, and Th17-like cells were increased and more clonally expanded in severe COVID-19 patients. Patients' peripheral T cells showed no sign of exhaustion or augmented cell death, whereas T cells in BALFs produced higher levels of IFNG, TNF, CCL4, CCL5, etc. Paired TCR tracking indicated abundant recruitment of peripheral T cells to the severe patients' lung. Together, this study comprehensively depicts how the immune cell landscape is perturbed in severe COVID-19.

Reference

https://www.nature.com/articles/s41421-020-00225-2

CoVidAffect, real-time monitoring of mood variations following the COVID-19 outbreak in Spain

Abstract

The COVID-19 outbreak and the ensuing confinement measures are expected to bear a significant psychological impact on the affected populations. To date, all available studies designed to investigate the psychological effects of this unprecedented global crisis are based on cross-sectional surveys that do not capture emotional variations over time. Here, the data presented from CoVidAffect, a nationwide citizen science project, was aimed to provide longitudinal data of mood changes following the COVID-19 outbreak in the spanish territory. Spain is among the most affected countries by the pandemic, with one of the most restrictive and prolonged lockdowns worldwide. The project also collected a baseline of demographic and socioeconomic data. These data can be further analyzed to quantify emotional responses to specific measures and policies, and to understand the effect of context variables on psychological resilience. Importantly, this is the first dataset that offers the opportunity to study the behavior of emotion dynamics in a prolonged lockdown situation.

Reference

https://www.nature.com/articles/s41597-020-00700-1

A pragmatic randomized controlled trial reports lack of efficacy of hydroxychloroquine on coronavirus disease 2019 viral kinetics

Abstract

Here, 53 patients hospitalized with coronavirus disease 2019 (COVID-19) were randomized to hydroxychloroquine therapy (at a dose of 400 mg twice daily for seven days) in addition to standard care or standard care alone (ClinicalTrials.gov Identifier, NCT04316377). All severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) positive patients 18 years of age or older were eligible for study inclusion if they had moderately severe COVID-19 at admission. Treatment with hydroxychloroquine did not result in a significantly greater rate of decline in SARS-CoV-2 oropharyngeal viral load

compared to standard care alone during the first five days. The results suggest no important antiviral effect of hydroxychloroquine in humans infected with SARS-CoV-2.

Reference

https://www.nature.com/articles/s41467-020-19056-6

Development of humanized tri-specific nanobodies with potent neutralization for SARS-CoV-2

Abstract

SARS-CoV-2 is a newly emergent coronavirus, which has adversely impacted human health and has led to the COVID-19 pandemic. There is an unmet need to develop therapies against SARS-CoV-2 due to its severity and lack of treatment options. A promising approach to combat COVID-19 is through the neutralization of SARS-CoV-2 by therapeutic antibodies. Previously, a strategy was described to rapidly identify and generate llama nanobodies (VHH) from naïve and synthetic humanized VHH phage libraries that specifically bind the S1 SARS-CoV-2 spike protein, and block the interaction with the human ACE2 receptor. In this study, computer-aided design was used to construct multi-specific VHH antibodies fused to human IgG1 Fc domains based on the epitope predictions for leading VHHs. The resulting tri-specific VHH-Fc antibodies show more potent S1 binding, S1/ACE2 blocking, and SARS-CoV-2 pseudovirus neutralization than the bi-specific VHH-Fcs or combination of individual monoclonal VHH-Fcs. Furthermore, protein stability analysis of the VHH-Fcs shows favorable developability features, which enable them to be quickly and successfully developed into therapeutics against COVID-19.

Reference

https://www.nature.com/articles/s41598-020-74761-y

Expression of SARS-CoV-2 entry factors in lung epithelial stem cells and its potential implications for COVID-19

Abstract

SARS-CoV-2 can infiltrate the lower respiratory tract, resulting in severe respiratory failure and a high death rate. Normally, the airway and alveolar epithelium can be rapidly reconstituted by multipotent stem cells after episodes of infection. Here, we analyzed published RNA-seq datasets and demonstrated that cells of four different lung epithelial stem cell types express SARS-CoV-2 entry factors, including Ace2. Thus, stem cells can be potentially infected by SARS-CoV-2, which may lead to defects in regeneration capacity partially accounting for the severity of SARS-CoV-2 infection and its consequences.

Reference

https://www.nature.com/articles/s41598-020-74598-5

Bi-paratopic and multivalent VH domains block ACE2 binding and neutralize SARS-CoV-2

Abstract

Severe Neutralizing agents against SARS-CoV-2 are urgently needed for the treatment and prophylaxis of COVID-19. Here, a strategy was presented to rapidly identify and assemble synthetic human variable heavy (VH) domains toward neutralizing epitopes. We constructed a VH-phage library and targeted the angiotensin-converting enzyme 2 (ACE2) binding interface of the SARS-CoV-2 Spike receptor-binding domain (Spike-RBD). Using a masked selection approach, we identified VH binders to two non-overlapping epitopes and further assembled these into multivalent and bi-paratopic formats. These VH constructs showed increased affinity to Spike (up to 600-fold) and neutralization potency (up to 1,400-fold) on pseudotyped SARS-CoV-2 virus when compared to standalone VH domains. The most potent binder, a trivalent VH, neutralized authentic SARS-CoV-2 with a half-maximal inhibitory concentration (IC50) of 4.0 nM (180 ng ml−1). A cryo-EM structure of the trivalent VH bound to Spike shows

each VH domain engaging an RBD at the ACE2 binding site, confirming our original design strategy.

Reference

https://www.nature.com/articles/s41589-020-00679-1

Point mutation bias in SARS-CoV-2 variants results in increased ability to stimulate inflammatory responses

Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection induces severe pneumonia and is the cause of a worldwide pandemic. Coronaviruses, including SARS-CoV-2, have RNA proofreading enzymes in their genomes, resulting in fewer gene mutations than other RNA viruses. Nevertheless, variants of SARS-CoV-2 exist and may induce different symptoms; however, the factors and the impacts of these mutations are not well understood. It was found that there is a bias to the mutations occurring in SARS-CoV-2 variants, with disproportionate mutation to uracil (U). These point mutations to U are mainly derived from cytosine (C), which is consistent with the substrate specificity of host RNA editing enzymes, APOBECs. It was also found the point mutations which are consistent with other RNA editing enzymes, ADARs. For the C-to-U mutations, the context of the upstream uracil and downstream guanine from mutated position was found to be most prevalent. Further, the degree of increase of U in SARS-CoV-2 variants correlates with enhanced production of cytokines, such as TNF-α and IL-6, in cell lines when compared with stimulation by the ssRNA sequence of the isolated virus in Wuhan. Therefore, RNA editing is a factor for mutation bias in SARS-CoV-2 variants, which affects host inflammatory cytokines production.

Reference

https://www.nature.com/articles/s41598-020-74843-x

Unbiased screens show $CD8^+$ T cells of COVID-19 patients recognize shared epitopes in SARS-CoV-2, most of which are not located in the Spike protein

Abstract

Developing effective strategies to prevent or treat COVID-19 requires understanding the natural immune response to SARS-CoV-2. We used an unbiased, genome-wide screening technology to determine the precise peptide sequences in SARS-CoV-2 that are recognized by the memory $CD8^+$ T cells of COVID-19 patients. In total, we identified 3–8 epitopes for each of the six most prevalent human leukocyte antigen (HLA) types. These epitopes were broadly shared across patients and located in regions of the virus that are not subject to mutational variation. Notably, only 3 of the 29 shared epitopes were located in the spike protein, whereas most epitopes were located in ORF1ab or the nucleocapsid protein. We also found that $CD8^+$ T cells generally do not cross-react with epitopes in the four seasonal coronaviruses that cause the common cold. Overall, these findings can inform development of next-generation vaccines that better recapitulate natural $CD8^+$ T cell immunity to SARS-CoV-2.

Reference

https://www.cell.com/immunity/fulltext/S1074-7613(20)30447-7

Structure-Altering Mutations of the SARS-CoV-2 Frame Shifting RNA Element

Abstract

With the rapid rate of Covid-19 infections and deaths, treatments and cures besides hand washing, social distancing, masks, isolation, and quarantines are urgently needed. The treatments and vaccines rely on the basic biophysics of the complex viral apparatus. While proteins are serving as main drug and vaccine targets, therapeutic approaches targeting the 30,000 nucleotide RNA viral genome form important complementary approaches. Indeed, the high conservation of the viral genome, its close evolutionary relationship to other viruses, and the rise of gene editing and RNA-based vaccines all argue for a focus on the RNA agent itself. One of the key steps in the viral replication cycle inside host cells is the ribosomal frameshifting required for translation of overlapping open reading frames. The RNA frameshifting element (FSE), one of

three highly conserved regions of coronaviruses, is believed to include a pseudoknot considered essential for this ribosomal switching. In this work, we apply our graph-theory-based framework for representing RNA secondary structures, “RAG” (RNA-As Graphs), to alter key structural features of the FSE of the SARS-CoV-2 virus. Specifically, using RAG machinery of genetic algorithms for inverse folding adapted for RNA structures with pseudoknots, we computationally predict minimal mutations that destroy a structurally-important stem and/or the pseudoknot of the FSE, potentially dismantling the virus against translation of the polyproteins. Our microsecond molecular dynamics simulations of mutant structures indicate relatively stable secondary structures. These findings not only advance our computational design of RNAs containing pseudoknots; they pinpoint to key residues of the SARS-CoV-2 virus as targets for anti-viral drugs and gene editing approaches.

Reference

https://www.cell.com/biophysj/fulltext/S0006-3495(20)30814-6

High-density amplicon sequencing identifies community spread and ongoing evolution of SARS-CoV-2 in the Southern United States

Abstract

SARS-CoV-2 is constantly evolving. Prior studies focused on high case-density locations, such as the U.S. Northern and Western metropolitan areas. This study demonstrates continued SARS-CoV-2 evolution in a suburban Southern U.S. region by high-density amplicon sequencing of symptomatic cases. 57% of strains carried the spike D614G variant, which was associated with higher genome copy numbers and its prevalence expanded with time. Four strains carried a deletion in a predicted stem loop of the 3’ untranslated region. The data are consistent with community spread within local populations and the larger continental U.S. The data instill confidence in current testing sensitivity and validate “testing by sequencing” as an option to uncover cases, particularly non-standard COVID-19 clinical presentations. This study contributes to the understanding of COVID-19 through an extensive set of genomes from a non-urban setting and informs vaccine design by defining D614G as a dominant and emergent SARS-CoV-2 isolate in the U.S.

Reference

https://www.cell.com/cell-reports/fulltext/S2211-1247(20)31341-3

Plasma proteomics identify biomarkers and pathogenesis of COVID-19

Abstract

The COVID-19 pandemic is a global public health crisis. However, little is known about the pathogenesis and biomarkers of COVID-19. Herein, we profiled host responses to COVID-19 by performing plasma proteomics of a cohort of COVID-19 patients including non-survivors and survivors recovered from mild or severe symptoms, and uncovered numerous COVID-19-associated alterations of plasma proteins. A machine learning-based was developed, pipeline to identify 11 proteins as biomarkers and a set of biomarker combinations, which were validated by an independent cohort and accurately distinguished and predicted COVID-19 outcomes. Some of the biomarkers were further validated by ELISA using a larger cohort. These markedly altered proteins, including the biomarkers mediate pathophysiological pathways such as immune or inflammatory responses, platelet degranulation and coagulation, and metabolism, that likely contribute to the pathogenesis. The findings provide valuable knowledge about COVID-19 biomarkers, and shed light on the pathogenesis and potential therapeutic targets of COVID-19.

Reference

https://www.cell.com/immunity/fulltext/S1074-7613(20)30449-0

Coxsackievirus B type 4 infection in β cells downregulates the chaperone prefoldin uri to induce a MODY4-like diabetes *via* PDX1 silencing

Abstract

Enteroviruses are suspected to contribute to insulin-producing β cell loss and hyperglycemia-induced diabetes. However, mechanisms are not fully defined. Here, it was shown that coxsackievirus B type 4 (CVB4) infection in human islet-engrafted mice and in rat insulinoma cells displays loss of unconventional prefoldin RPB5 interactor (URI) and PDX1, affecting β cell function and identity. Genetic URI ablation in the

mouse pancreas causes PDX1 depletion in β cells. Importantly, diabetic PDX1 heterozygous mice overexpressing URI in β cells are more glucose tolerant. Mechanistically, URI loss triggers estrogen receptor nuclear translocation leading to DNA methyltransferase 1 (DNMT1) expression, which induces Pdx1 promoter hypermethylation and silencing. Consequently, demethylating agent procainamide-mediated DNMT1 inhibition reinstates PDX1 expression and protects against diabetes in pancreatic URI-depleted mice . Finally, the β cells of human diabetes patients show correlations between viral protein 1 and URI, PDX1, and DNMT1 levels. URI and DNMT1 expression and PDX1 silencing provide a causal link between enterovirus infection and diabetes.

Reference

https://www.cell.com/cell-reports-medicine/fulltext/S2666-3791(20)30167-1

Genome-wide CRISPR screens reveal host factors critical for SARS-CoV-2 infection

Abstract

Identification of host genes essential for SARS-CoV-2 infection may reveal novel therapeutic targets and inform our understanding of COVID-19 pathogenesis. Here, genome-wide CRISPR screens in Vero-E6 cells with SARS-CoV-2 were performed, MERS-CoV, bat coronavirus HKU5 expressing the SARS-CoV-1 spike, and VSV expressing the SARS-CoV-2 spike. It was identified known SARS-CoV-2 host factors including the receptor ACE2 and protease Cathepsin L. It was additionally discovered pro-viral genes and pathways including HMGB1 and the SWI/SNF chromatin remodeling complex that are SARS-lineage and pan-coronavirus specific, respectively. It was shown that HMGB1 regulates ACE2 expression and is critical for viral entry of SARS-CoV-2, SARS-CoV-1, and NL63. It was also shown that small molecule antagonists of identified gene products inhibited SARS-CoV-2 infection in monkey and human cells, demonstrating the conserved role of these genetic hits across species. Together this identifies potential therapeutic targets for SARS-CoV-2 and reveals SARS-lineage specific and pan-coronavirus host factors that regulate susceptibility to highly pathogenic coronaviruses.

Reference

https://www.cell.com/cell/fulltext/S0092-8674(20)31392-1

Publication Date: Oct 19, 2020

Evidence of protective role of Ultraviolet-B (UVB) radiation in reducing COVID-19 deaths

Abstract

Prior studies indicate the protective role of Ultraviolet-B (UVB) radiation in human health, mediated by vitamin D synthesis. In this observational study, a negative association of UVB radiation was empirically outlined as measured by ultraviolet index (UVI) with the number of COVID-19 deaths. A fixed-effect log-linear regression model was applied to a panel dataset of 152 countries over 108 days ($n = 6524$). The cumulative number of COVID-19 deaths and case-fatality rate (CFR) were used as the main dependent variables and isolate the UVI effect from potential confounding factors. After controlling for time-constant and time-varying factors, it was found that a permanent unit increase in UVI is associated with a 1.2 percentage points decline in daily growth rates of cumulative COVID-19 deaths [$p < 0.01$] and a 1.0 percentage points decline in the CFR daily growth rate [$p < 0.05$]. These results represent a significant percentage reduction in terms of daily growth rates of cumulative COVID-19 deaths (− 12%) and CFR (− 38%). A significant negative association was found between UVI and COVID-19 deaths, indicating evidence of the protective role of UVB in mitigating COVID-19 deaths. If confirmed *via* clinical studies, then the possibility of mitigating COVID-19 deaths via sensible sunlight exposure or vitamin D intervention would be very attractive.

Reference

https://www.nature.com/articles/s41598-020-74825-z

Immunity, endothelial injury and complement-induced coagulopathy in COVID-19

Abstract

In December 2019, a novel coronavirus was isolated from the respiratory epithelium of patients with unexplained pneumonia in Wuhan, China. This pathogen, named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), causes a pathogenic condition that has been termed coronavirus disease 2019 (COVID-19) and has reached pandemic proportions. As of 17 September 2020, more than 30 million confirmed SARS-CoV-2 infections have been reported in 204 different countries, claiming more than 1 million lives worldwide. Accumulating evidence suggests that SARS-CoV-2 infection can lead to a variety of clinical conditions, ranging from asymptomatic to life-threatening cases. In the early stages of the disease, most patients experience mild clinical symptoms, including a high fever and dry cough. However, 20% of patients rapidly progress to severe illness characterized by atypical interstitial bilateral pneumonia, acute respiratory distress syndrome and multiorgan dysfunction. Almost 10% of these critically ill patients subsequently die. Insights into the pathogenic mechanisms underlying SARS-CoV-2 infection and COVID-19 progression are emerging and highlight the critical role of the immunological hyper-response — characterized by widespread endothelial damage, complement-induced blood clotting and systemic microangiopathy — in disease exacerbation. These insights may aid the identification of new or existing therapeutic interventions to limit the progression of early disease and treat severe cases.

Reference

https://www.nature.com/articles/s41581-020-00357-4

Multiple myeloma and SARS-CoV-2 infection: Clinical characteristics and prognostic factors of inpatient mortality

Abstract

There is limited information on the characteristics, prognostic factors, and outcomes of patients with multiple myeloma (MM) hospitalized with COVID-19. This retrospective case series investigated 167 patients reported from 73 hospitals within the Spanish

Myeloma Collaborative Group network in March and April, 2020. Outcomes were compared with 167 randomly selected, contemporary, age-/sex-matched noncancer patients with COVID-19 admitted at six participating hospitals. Among MM and noncancer patients, median age was 71 years, and 57% of patients were male; 75 and 77% of patients, respectively, had at least one comorbidity. COVID-19 clinical severity was moderate–severe in 77 and 89% of patients and critical in 8 and 4%, respectively. Supplemental oxygen was required by 47 and 55% of MM and noncancer patients, respectively, and 21%/9% vs 8%/6% required noninvasive/invasive ventilation. Inpatient mortality was 34 and 23% in MM and noncancer patients, respectively. Among MM patients, inpatient mortality was 41% in males, 42% in patients aged >65 years, 49% in patients with active/progressive MM at hospitalization, and 59% in patients with comorbid renal disease at hospitalization, which were independent prognostic factors on adjusted multivariate analysis. This case series demonstrates the increased risk and identifies predictors of inpatient mortality among MM patients hospitalized with COVID-19.

Reference

https://www.nature.com/articles/s41408-020-00372-5

Reduced numbers of T cells and B cells correlates with persistent SARS-CoV-2 presence in non-severe COVID-19 patients

Abstract

COVID-19 has been widely spreading. It was aimed to examine adaptive immune cells in non-severe patients with persistent SARS-CoV-2 shedding. 37 non-severe patients with persistent SARS-CoV-2 presence that were transferred to Zhongnan hospital of Wuhan University were retrospectively recruited to the PP (persistently positive) group, which was further allocated to PPP group (n = 19) and PPN group (n = 18), according to their testing results after 7 days (N = negative). Epidemiological, demographic, clinical and laboratory data were collected and analyzed. Data from age- and sex-matched non-severe patients at disease onset (PA [positive on admission] patients, n = 37), and lymphocyte subpopulation measurements from matched 54 healthy subjects were extracted for comparison (HC). Compared with PA patients, PP patients had much

improved laboratory findings. The absolute numbers of CD3+ T cells, CD4+ T cells, and NK cells were significantly higher in PP group than that in PA group, and were comparable to that in healthy controls. PPP subgroup had markedly reduced B cells and T cells compared to PPN group and healthy subjects. Finally, paired results of these lymphocyte subpopulations from 10 PPN patients demonstrated that the number of T cells and B cells significantly increased when the SARS-CoV-2 tests turned negative. Persistent SARS-CoV-2 presence in non-severe COVID-19 patients is associated with reduced numbers of adaptive immune cells. Monitoring lymphocyte subpopulations could be clinically meaningful in identifying fully recovered COVID-19 patients.

Reference

https://www.nature.com/articles/s41598-020-73955-8

Rational approach toward COVID-19 main protease inhibitors *via* molecular docking, molecular dynamics simulation and free energy calculation

Abstract

In the rapidly evolving coronavirus disease (COVID-19) pandemic, repurposing existing drugs and evaluating commercially available inhibitors against druggable targets of the virus could be an effective strategy to accelerate the drug discovery process. The 3C-Like proteinase (3CLpro) of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been identified as an important drug target due to its role in viral replication. The lack of a potent 3CLpro inhibitor and the availability of the X-ray crystal structure of 3CLpro (PDB-ID 6LU7) motivated us to perform computational studies to identify commercially available potential inhibitors. A combination of modeling studies was performed to identify potential 3CLpro inhibitors from the protease inhibitor database MEROPS (https://www.ebi.ac.uk/merops/index.shtml). Binding energy evaluation identified key residues for inhibitor design. We found 15 potential 3CLpro inhibitors with higher binding affinity than that of an α-ketoamide inhibitor determined via X-ray structure. Among them, saquinavir and three other investigational drugs aclarubicin, TMC-310911, and faldaprevir could be suggested as potential 3CLpro inhibitors. Further experimental investigation was recommended of these compounds.

Reference

https://www.nature.com/articles/s41598-020-74468-0

Rapid production of SARS-CoV-2 receptor binding domain (RBD) and spike specific monoclonal antibody CR3022 in *Nicotiana benthamiana*

Abstract

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is responsible for the ongoing global outbreak of coronavirus disease (COVID-19) which is a significant threat to global public health. The rapid spread of COVID-19 necessitates the development of cost-effective technology platforms for the production of vaccines, drugs, and protein reagents for appropriate disease diagnosis and treatment. In this study, we explored the possibility of producing the receptor binding domain (RBD) of SARS-CoV-2 and an anti-SARS-CoV monoclonal antibody (mAb) CR3022 in Nicotiana benthamiana. Both RBD and mAb CR3022 were transiently produced with the highest expression level of 8 µg/g and 130 µg/g leaf fresh weight respectively at 3 days post-infiltration. The plant-produced RBD exhibited specific binding to the SARS-CoV-2 receptor, angiotensin-converting enzyme 2 (ACE2). Furthermore, the plant-produced mAb CR3022 binds to SARS-CoV-2, but fails to neutralize the virus in vitro. This is the first report showing the production of anti-SARS-CoV-2 RBD and mAb CR3022 in plants. Overall these findings provide a proof-of-concept for using plants as an expression system for the production of SARS-CoV-2 antigens and antibodies or similar other diagnostic reagents against SARS-CoV-2 rapidly, especially during epidemic or pandemic situation.

Reference

https://www.nature.com/articles/s41598-020-74904-1

Interferons and viruses induce a novel truncated ACE2 isoform and not the full-length SARS-CoV-2 receptor

Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes COVID-19, utilizes angiotensin-converting enzyme 2 (ACE2) for entry into target cells. ACE2 has been proposed as an interferon-stimulated gene (ISG). Thus, interferon-

induced variability in ACE2 expression levels could be important for susceptibility to COVID-19 or its outcomes. Here, we report the discovery of a novel, transcriptionally independent truncated isoform of ACE2, which we designate as deltaACE2 (dACE2). We demonstrate that dACE2, but not ACE2, is an ISG. In The Cancer Genome Atlas, the expression of dACE2 was enriched in squamous tumors of the respiratory, gastrointestinal and urogenital tracts. In vitro, dACE2, which lacks 356 amino-terminal amino acids, was non-functional in binding the SARS-CoV-2 spike protein and as a carboxypeptidase. Our results suggest that the ISG-type induction of dACE2 in IFN-high conditions created by treatments, an inflammatory tumor microenvironment or viral co-infections is unlikely to increase the cellular entry of SARS-CoV-2 and promote infection.

Reference

https://www.nature.com/articles/s41588-020-00731-9

Molecular docking study of potential phytochemicals and their effects on the complex of SARS-CoV2 spike protein and human ACE2

Abstract

Angiotensin converting enzyme 2 (ACE2) (EC:3.4.17.23) is a transmembrane protein which is considered as a receptor for spike protein binding of novel coronavirus (SARS-CoV2). Since no specific medication is available to treat COVID-19, designing of new drug is important and essential. In this regard, in silico method plays an important role, as it is rapid and cost effective compared to the trial and error methods using experimental studies. Natural products are safe and easily available to treat coronavirus affected patients, in the present alarming situation. In this paper five phytochemicals, which belong to flavonoid and anthraquinone subclass, have been selected as small molecules in molecular docking study of spike protein of SARS-CoV2 with its human receptor ACE2 molecule. Their molecular binding sites on spike protein bound structure with its receptor have been analyzed. From this analysis, hesperidin, emodin and chrysin are selected as competent natural products from both Indian and Chinese medicinal plants, to treat COVID-19. Among them, the phytochemical hesperidin can bind with ACE2 protein and bound structure of ACE2 protein and spike protein of

SARS-CoV2 noncompetitively. The binding sites of ACE2 protein for spike protein and hesperidin, are located in different parts of ACE2 protein. Ligand spike protein causes conformational change in three-dimensional structure of protein ACE2, which is confirmed by molecular docking and molecular dynamics studies. This compound modulates the binding energy of bound structure of ACE2 and spike protein. This result indicates that due to presence of hesperidin, the bound structure of ACE2 and spike protein fragment becomes unstable. As a result, this natural product can impart antiviral activity in SARS CoV2 infection. The antiviral activity of these five natural compounds are further experimentally validated with QSAR study.

Reference

https://www.nature.com/articles/s41598-020-74715-4

Estimating the infection-fatality risk of SARS-CoV-2 in New York City during the spring 2020 pandemic wave: A model-based analysis

Abstract

Background: As the COVID-19 pandemic continues to unfold, the infection-fatality risk (ie, risk of death among all infected individuals including those with asymptomatic and mild infections) is crucial for gauging the burden of death due to COVID-19 in the coming months or years. Here, the infection-fatality risk of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in New York City, NY, USA, the first epidemic centre in the USA, was estimated where the infection-fatality risk remains unclear.

Methods: In this model-based analysis, we developed a meta-population network model-inference system to estimate the underlying SARS-CoV-2 infection rate in New York City during the 2020 spring pandemic wave using available case, mortality, and mobility data. Based on these estimates, the infection-fatality risk for all ages overall and for five age groups (<25, 25–44, 45–64, 65–74, and ≥75 years) were further estimated separately, during the period March 1 to June 6, 2020 (i.e., before the city began a phased reopening).

Findings: During the period March 1 to June 6, 2020, 205 639 people had a laboratory-confirmed infection with SARS-CoV-2 and 21 447 confirmed and probable COVID-19-

related deaths occurred among residents of New York City. An overall infection-fatality risk of 1·39% (95% credible interval 1·04–1·77) in New York City was estimated. Our estimated infection-fatality risk for the two oldest age groups (65–74 and ≥75 years) was much higher than the younger age groups, with a cumulative estimated infection-fatality risk of 0·116% (0·0729–0·148) for those aged 25–44 years and 0·939% (0·729–1·19) for those aged 45–64 years versus 4·87% (3·37–6·89) for those aged 65–74 years and 14·2% (10·2–18·1) for those aged 75 years and older. In particular, weekly infection-fatality risk was estimated to be as high as 6·72% (5·52–8·01) for those aged 65–74 years and 19·1% (14·7–21·9) for those aged 75 years and older.

Interpretation: The results are based on more complete ascertainment of COVID-19-related deaths in New York City than other places and thus probably reflect the true higher burden of death due to COVID-19 than that previously reported elsewhere. Given the high infection-fatality risk of SARS-CoV-2, governments must account for and closely monitor the infection rate and population health outcomes and enact prompt public health responses accordingly as the COVID-19 pandemic unfolds.

Reference

https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30769-6/fulltext

Integrative transcriptome analyses empower the anti-COVID-19 drug arsenal

Abstract

The beginning of the twenty-first century has been marked by three distinct waves of zoonotic coronavirus outbreaks into the human population. The COVID-19 (Coronavirus disease 2019) pandemic is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and emerged as a global threat endangering the livelihoods of millions worldwide. Currently, and despite collaborative efforts, diverse therapeutic strategies from ongoing clinical trials are still debated. To address the need for such an immediate call of action, we leveraged the largest dataset of drug-induced transcriptomic perturbations, public SARS-CoV-2 transcriptomic datasets, and expression profiles from normal lung transcriptomes. Most importantly, our unbiased systems biology approach prioritized more than 50 repurposable drug candidates (e.g., Corticosteroids, Janus kinase and Bruton kinase inhibitors). Further clinical investigation of these FDA

approved candidates as monotherapy or in combination with an antiviral regimen (e.g., Remdesivir) could lead to promising outcomes in COVID-19 patients.

Reference

https://www.cell.com/iscience/fulltext/S2589-0042(20)30889-0

Publication Date: Oct 16, 2020

Automatic classification between COVID-19 pneumonia, non-COVID-19 pneumonia, and the healthy on chest X-ray image: Combination of data augmentation methods

Abstract

This study aimed to develop and validate computer-aided diagnosis (CXDx) system for classification between COVID-19 pneumonia, non-COVID-19 pneumonia, and the healthy on chest X-ray (CXR) images. From two public datasets, 1248 CXR images were obtained, which included 215, 533, and 500 CXR images of COVID-19 pneumonia patients, non-COVID-19 pneumonia patients, and the healthy samples, respectively. The proposed CADx system utilized VGG16 as a pre-trained model and combination of conventional method and mixup as data augmentation methods. Other types of pre-trained models were compared with the VGG16-based model. Single type or no data augmentation methods were also evaluated. Splitting of training/validation/test sets was used when building and evaluating the CADx system. Three-category accuracy was evaluated for test set with 125 CXR images. The three-category accuracy of the CAD system was 83.6% between COVID-19 pneumonia, non-COVID-19 pneumonia, and the healthy. Sensitivity for COVID-19 pneumonia was more than 90%. The combination of conventional method and mixup was more useful than single type or no data augmentation method. In conclusion, this study was able to create an accurate CADx system for the 3-category classification. Source code of our CADx system is available as open source for COVID-19 research.

Reference

https://www.nature.com/articles/s41598-020-74539-2

Whole blood immunophenotyping uncovers immature neutrophil-to-VD2 T-cell ratio as an early marker for severe COVID-19

Abstract

SARS-CoV-2 is the novel coronavirus responsible for the current COVID-19 pandemic. Severe complications are observed only in a small proportion of infected patients but the cellular mechanisms underlying this progression are still unknown. Comprehensive flow cytometry of whole blood samples from 54 COVID-19 patients reveals a dramatic increase in the number of immature neutrophils. This increase strongly correlates with disease severity and is associated with elevated IL-6 and IP-10 levels, two key players in the cytokine storm. The most pronounced decrease in cell counts is observed for CD8 T-cells and VD2 γδ T-cells, which both exhibit increased differentiation and activation. ROC analysis reveals that the count ratio of immature neutrophils to VD2 (or CD8) T-cells predicts pneumonia onset (0.9071) as well as hypoxia onset (0.8908) with high sensitivity and specificity. It would thus be a useful prognostic marker for preventive patient management and improved healthcare resource management.

Reference

https://www.nature.com/articles/s41467-020-19080-6

Individuals with Down syndrome hospitalized with COVID-19 have more severe disease

Abstract

Purpose: Rare genetic conditions like Down syndrome (DS) are historically understudied. Infection is a leading cause of mortality in DS, along with cardiac anomalies. Currently, it is unknown how the COVID-19 pandemic affects individuals with DS. Herein, we report an analysis of individuals with DS who were hospitalized with COVID-19 in New York, New York, USA.

Methods: In this retrospective, dual-center study of 7246 patients hospitalized with COVID-19, we analyzed all patients with DS admitted in the Mount Sinai Health System

and Columbia University Irving Medical Center. Hospitalization rates, clinical characteristics, and outcomes were assessed.

Results: 12 Patients with DS were identified. Hospitalized individuals with DS are on average ten years younger than patients without DS. Patients with DS have more severe disease than controls, particularly an increased incidence of sepsis and mechanical ventilation.

Conclusion: It was demonstrated that individuals with DS who are hospitalized with COVID-19 are younger than their non-DS counterparts, and that they have more severe disease than age-matched controls. It was concluded that particular care should be considered for both the prevention and treatment of COVID-19 in these patients.

Reference

https://www.nature.com/articles/s41436-020-01004-w

Development of a prognostic model for mortality in COVID-19 infection using machine learning

Abstract

Coronavirus disease 2019 (COVID-19) is a novel disease resulting from infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which has quickly risen since the beginning of 2020 to become a global pandemic. As a result of the rapid growth of COVID-19, hospitals are tasked with managing an increasing volume of these cases with neither a known effective therapy, an existing vaccine, nor well-established guidelines for clinical management. The need for actionable knowledge amidst the COVID-19 pandemic is dire and yet, given the urgency of this illness and the speed with which the healthcare workforce must devise useful policies for its management, there is insufficient time to await the conclusions of detailed, controlled, prospective clinical research. Thus, we present a retrospective study evaluating laboratory data and mortality from patients with positive RT-PCR assay results for SARS-CoV-2. The objective of this study is to identify prognostic serum biomarkers in patients at greatest risk of mortality. To this end, we develop a machine learning model using five serum chemistry laboratory parameters (c-reactive protein, blood urea nitrogen, serum calcium, serum albumin, and lactic acid) from 398 patients (43 expired and 355 non-

expired) for the prediction of death up to 48 h prior to patient expiration. The resulting support vector machine model achieved 91% sensitivity and 91% specificity (AUC 0.93) for predicting patient expiration status on held-out testing data. Finally, we examine the impact of each feature and feature combination in light of different model predictions, highlighting important patterns of laboratory values that impact outcomes in SARS-CoV-2 infection.

Reference

https://www.nature.com/articles/s41379-020-00700-x

Clinical characteristics and survival analysis in critical and non-critical patients with COVID-19 in Wuhan, China: A single-center retrospective case control study

Abstract

Since the outbreak of COVID-19 in China at the end of 2019, the world has experienced a large-scale epidemic caused by the SARS-CoV-2. The epidemiological and clinical course of COVID-19 patients has been reported, but there have been few analyses about the characteristics, predictive risk factors, and outcomes of critical patients. In this single-center retrospective case–control study, 90 adult inpatients hospitalized at Tongji Hospital (Wuhan, China) were included. Demographic, clinical, laboratory tests, and treatment data were obtained and compared between critical and non-critical patients. We found that compared with non-critical patients, the critical patients had higher SOFA score and qSOFA scores. Critical patients had lower lymphocyte and platelet count, elevated D-dimer, decreased fibrinogen, and elevated high-sensitivity C-reactive protein (hsCRP), and interleukin-6(IL-6). More critical patients received treatment including antibiotics, anticoagulation, corticosteroid, and oxygen therapy than non-critical ones. Multivariable regression showed higher qSOFA score and elevation of IL-6 were related to critical patients. Antibiotic usage and anticoagulation were associated with decreased in-hospital mortality. And critical grouping contributed greatly to in-hospital death. Critical COVID-19 patients have a more severe clinical course. qSOFA score and elevation of IL-6 are risk factors for critical condition. Non-critical grouping, positive antibiotic application, and anticoagulation may be beneficial for patient survival.

Reference

https://www.nature.com/articles/s41598-020-74465-3

Rabies virus-based COVID-19 vaccine CORAVAX™ induces high levels of neutralizing antibodies against SARS-CoV-2

Abstract

The recently emerged coronavirus SARS-CoV-2, the causative agent of COVID-19, is rapidly spreading in the world. The exponentially expanding threat of SARS-CoV-2 to global health highlights the urgent need for a vaccine. Herein, the rapid development of a novel, highly efficient, and safe COVID-19 vaccine was shown using a rabies virus-based vector that has proven to be an efficient vaccine against several emerging infectious diseases. This study reports that both a live and an inactivated rabies virus containing the SARS-CoV-2 spike S1 protein induces potent virus-neutralizing antibodies at much higher levels than seen in the sera of convalescent patients. In summary, the results provided here warrant further development of this safe and established vaccine platform against COVID-19.

Reference

https://www.nature.com/articles/s41541-020-00248-6

Quantifying the adhesive strength between the SARS-CoV-2 S-proteins and human receptor and its effect in therapeutics

Abstract

The binding affinity and adhesive strength between the spike (S) glycoproteins of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and the human angiotensin-converting enzyme 2 (ACE2) receptor is computed using molecular dynamics (MD) simulations. The calculations indicate that the binding affinity is e_{RS} = 12.6 ± 1 kCal·mol^{-1} with a maximum adhesive force of ∼102 pN. The analysis suggests that only 27 (13 in S-protein, 14 in ACE2) residues are active during the initial fusion process between the S-protein and ACE2 receptor. With these insights, the effect of possible therapeutics was investigated in the size and wrapping time of virus particles

by reducing the binding energy. The analysis indicates that this energy has to be reduced significantly, around 50% or more, to block SARS-CoV-2 particles with radius in the order of R ≤ 60 nm. The study provides concise target residues and target binding energy reduction between S-proteins and receptors for the development of new therapeutics treatments for COVID-19 guided by computational design.

Reference

https://www.nature.com/articles/s41598-020-74189-4

Cytokine elevation in severe and critical COVID-19: As rapid systematic review, meta-analysis, and comparison with other inflammatory syndromes

Abstract

The description of a so-called cytokine storm in patients with COVID-19 has prompted consideration of anti-cytokine therapies, particularly interleukin-6 antagonists. However, direct systematic comparisons of COVID-19 with other critical illnesses associated with elevated cytokine concentrations have not been reported. In this Rapid Review, we report the results of a systematic review and meta-analysis of COVID-19 studies published or posted as preprints between Nov 1, 2019, and April 14, 2020, in which interleukin-6 concentrations in patients with severe or critical disease were recorded. 25 COVID-19 studies (n=1245 patients) were ultimately included. Comparator groups included four trials each in sepsis (n=5320), cytokine release syndrome (n=72), and acute respiratory distress syndrome unrelated to COVID-19 (n=2767). In patients with severe or critical COVID-19, the pooled mean serum interleukin-6 concentration was 36·7 pg/mL (95% CI 21·6–62·3 pg/mL; I2=57·7%). Mean interleukin-6 concentrations were nearly 100 times higher in patients with cytokine release syndrome (3110·5 pg/mL, 632·3–15 302·9 pg/mL; p<0·0001), 27 times higher in patients with sepsis (983·6 pg/mL, 550·1–1758·4 pg/mL; p<0·0001), and 12 times higher in patients with acute respiratory distress syndrome unrelated to COVID-19 (460 pg/mL, 216·3–978·7 pg/mL; p<0·0001). Our findings question the role of a cytokine storm in COVID-19-induced organ dysfunction. Many questions remain about the immune features of COVID-19 and the potential role of anti-cytokine and immune-modulating treatments in patients with the disease.

Reference

https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30404-5/fulltext

Quantitative assessment of olfactory dysfunction accurately detects asymptomatic COVID-19 carriers

Abstract

Background: COVID-19 threatens the global community because a large fraction of infected people are asymptomatic, yet can effectively transmit SARS-CoV-2. Finding and isolating these silent carriers is a crucial step in confining the spread of the disease. A sudden loss of the sense of smell has been self-reported by COVID-19 patients across different countries, consistent with expression of the molecular factors mediating SARS-CoV-2 uptake into human olfactory epithelial supporting cells. However, precise quantification of olfactory loss in asymptomatic COVID-19 carriers is missing to date.

Methods: To quantify olfactory functions in asymptomatic COVID-19 patients, an olfactory-action meter was designed that determines detectability indices at different odor concentrations and an olfactory matching accuracy score using monomolecular odors. The optimization of test parameters allowed us to reliably and accurately assess olfactory deficits in a patient within 20 minutes.

Findings: Measurement of detection indices at low concentrations revealed a 50% reduction in asymptomatic COVID-19 carriers. Further, patients with better detection scores showed significantly reduced olfactory matching accuracies compared to normal healthy subjects. The quantification of olfactory loss, considering all parameters, identified 82% of the asymptomatic SARS-CoV-2 carriers with olfactory deficits. However, on subjective evaluation, only 15% of the patients noticed a compromised ability to smell.

Interpretation: Compromised olfactory fitness can serve as a strong basis for identifying asymptomatic COVID-19 patients. Detailed design specifications and protocols provided here should enable the development of a sensitive, fast, and economical screening strategy that can be administered to large populations to prevent the rapid spread of COVID-19.

Reference

https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(20)30319-9/fulltext

Publication Date: Oct 15, 2020

Retinal involvement and ocular findings in COVID-19 pneumonia patients

Abstract

Changes in immune and coagulation systems and possible viral spread through the blood–brain barrier have been described in SARS-CoV-2 infection. In this study, the possible retinal involvement and ocular findings in severe COVID-19 pneumonia patients was evaluated. A cross-sectional study was conducted on 46 patients affected by severe COVID-19 who were hospitalized in one intensive care unit (ICU) and in two infectious disease wards, including bedside eye screening, corneal sensitivity assessment and retinography. A total of 43 SARS-CoV-2-positive pneumonia patients affected with COVID-19 pneumonia were included, including 25 males and 18 females, with a median age of 70 years [IQR 59–78]. Except for one patient with unilateral posterior chorioretinitis of opportunistic origin, of whom aqueous tap was negative for SARS-CoV-2, no further retinal manifestation related to COVID-19 infection was found in our cohort. We found 3 patients (7%) with bilateral conjunctivitis in whom PCR analysis on conjunctival swabs provided negative results for SARS-CoV-2. No alterations in corneal sensitivity were found. We demonstrated the absence of retinal involvement in SARS-CoV-2 pneumonia patients. Ophthalmologic evaluation in COVID-19, particularly in patients hospitalized in an ICU setting, may be useful to reveal systemic co-infections by opportunistic pathogens.

Reference

https://www.nature.com/articles/s41598-020-74446-6

Pathological features of COVID-19-associated lung injury: A preliminary proteomics report based on clinical samples

Abstract

The COVID-19 pandemic has emerged as a global health emergency due to its association with severe pneumonia and relative high mortality. However, the molecular characteristics and pathological features underlying COVID-19 pneumonia remain largely unknown. To characterize molecular mechanisms underlying COVID-19 pathogenesis in the lung tissue using a proteomic approach, fresh lung tissues were obtained from newly deceased patients with COVID-19 pneumonia. After virus inactivation, a quantitative proteomic approach combined with bioinformatics analysis was used to detect proteomic changes in the SARS-CoV-2-infected lung tissues. We identified significant differentially expressed proteins involved in a variety of fundamental biological processes including cellular metabolism, blood coagulation, immune response, angiogenesis, and cell microenvironment regulation. Several inflammatory factors were upregulated, which was possibly caused by the activation of NF-κB signaling. Extensive dysregulation of the lung proteome in response to SARS-CoV-2 infection was discovered. Our results systematically outlined the molecular pathological features in terms of the lung response to SARS-CoV-2 infection, and provided the scientific basis for the therapeutic target that is urgently needed to control the COVID-19 pandemic.

Reference

https://www.nature.com/articles/s41392-020-00355-9

A nanoluciferase SARS-CoV-2 for rapid neutralization testing and screening of anti-infective drugs for COVID-19

Abstract

A high-throughput platform would greatly facilitate coronavirus disease 2019 (COVID-19) serological testing and antiviral screening. Here, a high-throughput nanoluciferase severe respiratory syndrome coronavirus 2 (SARS-CoV-2-Nluc) was presented that is genetically stable and replicates similarly to the wild-type virus in cell culture. SARS-

CoV-2-Nluc can be used to measure neutralizing antibody activity in patient sera within 5 hours, and it produces results in concordance with a plaque reduction neutralization test (PRNT). Additionally, using SARS-CoV-2-Nluc infection of A549 cells expressing human ACE2 receptor (A549-hACE2), we show that the assay can be used for antiviral screening. Using the optimized SARS-CoV-2-Nluc assay, a panel of antivirals and other anti-infective drugs was evaluate, and nelfinavir, rupintrivir, and cobicistat was identified as the most selective inhibitors of SARS-CoV-2-Nluc (EC_{50} 0.77 to 2.74 μM). In contrast, most of the clinically approved antivirals, including tenofovir alafenamide, emtricitabine, sofosbuvir, ledipasvir, and velpatasvir were inactive at concentrations up to 10 μM. Collectively, this high-throughput platform represents a reliable tool for rapid neutralization testing and antiviral screening for SARS-CoV-2.

Reference

https://www.nature.com/articles/s41467-020-19055-7

Statin use is associated with lower disease severity in COVID-19 infection

Abstract

It was aimed to study the association of hyperlipidemia and statin use with COVID-19 severity. We analysed a retrospective cohort of 717 patients admitted to a tertiary centre in Singapore for COVID-19 infection. Clinical outcomes of interest were oxygen saturation ≤ 94% requiring supplemental oxygen, intensive-care unit (ICU) admission, invasive mechanical-ventilation and death. Patients on long term dyslipidaemia medications (statins, fibrates or ezetimibe) were considered to have dyslipidaemia. Logistic regression models were used to study the association between dyslipidaemia and clinical outcomes adjusted for age, gender and ethnicity. Statin treatment effect was determined, in a nested case–control design, through logistic treatment models with 1:3 propensity matching for age, gender and ethnicity. All statistical tests were two-sided, and statistical significance was taken as $p < 0.05$. One hundred fifty-six (21.8%) patients had dyslipidaemia and 97% of these were on statins. Logistic treatment models showed a lower chance of ICU admission for statin users when compared to non-statin users (ATET: Coeff (risk difference): − 0.12 (− 0.23, − 0.01); $p = 0.028$). There were no other significant differences in other outcomes. Statin use was independently associated with

lower ICU admission. This supports current practice to continue prescription of statins in COVID-19 patients.

Reference

https://www.nature.com/articles/s41598-020-74492-0

Rapid genomic characterization of SARS-CoV-2 viruses from clinical specimens using nanopore sequencing

Abstract

The novel SARS-CoV-2 outbreak has swiftly spread worldwide. The rapid genome sequencing of SARS-CoV-2 strains has become a helpful tool for better understanding the genomic characteristics and origin of the virus. To obtain virus whole-genome sequences directly from clinical specimens, we performed nanopore sequencing using a modified ARTIC protocol in a portable nanopore sequencer and validated a routine 8-h workflow and a 5-h rapid pipeline. Some optimization was conducted to improve the genome sequencing workflow. The sensitivity of the workflow was also tested by serially diluting RNA from clinical samples. The optimized pipeline was finally applied to obtain the whole genomes of 29 clinical specimens collected in Hangzhou from January to March 2020. In the 29 obtained complete genomes of SARS-CoV-2, 33 variations were identified and analyzed. The genomic variations and phylogenetic analysis hinted at multiple sources and different transmission patterns during the COVID-19 epidemic in Hangzhou, China. In conclusion, the genomic characteristics and origin of the virus can be quickly determined by nanopore sequencing following our workflows.

Reference

https://www.nature.com/articles/s41598-020-74656-y

Synthesis and systematic review of reported neonatal SARS-CoV-2 infections

Abstract

A number of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infections have been reported in neonates. Here, it was aimed to clarify the transmission route,

clinical features and outcomes of these infections. A meta-analysis was presented of 176 published cases of neonatal SARS-CoV-2 infections that were defined by at least one positive nasopharyngeal swab and/or the presence of specific IgM. It was reported that 70% and 30% of infections are due to environmental and vertical transmission, respectively. The analysis showed that 55% of infected neonates developed COVID-19; the most common symptoms were fever (44%), gastrointestinal (36%), respiratory (52%) and neurological manifestations (18%), and lung imaging was abnormal in 64% of cases. A lack of mother–neonate separation from birth is associated with late SARS-CoV-2 infection (OR 4.94 (95% CI: 1.98–13.08), p = 0.0002; adjusted OR 6.6 (95% CI: 2.6–16), p < 0.0001), while breastfeeding is not (OR 0.35 (95% CI: 0.09–1.18), p = 0.10; adjusted OR 2.2 (95% CI: 0.7–6.5), p = 0.148). Our findings add to the literature on neonatal SARS-CoV-2 infections.

Reference

https://www.nature.com/articles/s41467-020-18982-9

Clinical characteristics and outcomes among hospitalized adults with severe COVID-19 admitted to a tertiary medical center and receiving antiviral, antimalarials, glucocorticoids, or immunomodulation with tocilizumab or cyclosporine: A retrospective observational study (COQUIMA cohort)

Abstract

Background: The COVID-19 outbreak challenges the Spanish health system since March 2020. Some available therapies (antimalarials, antivirals, biological agents) were grounded on clinical case observations or basic science data. The aim of this study is to describe the characteristics and impact of different therapies on clinical outcomes in a cohort of severe COVID-19 patients.

Methods: In this retrospective, single-center, observational study, sequential data on adult patients was collected admitted to Hospital Universitario Quironsalud Madrid. Eligible patients should have a microbiological (positive test on RT-PCR assay from a nasal swab) or an epidemiological diagnosis of severe COVID-19. Demographic, baseline comorbidities, laboratory data, clinical outcomes, and treatments were compared between survivors and non-survivors. We carried out univariate and

multivariate logistic regression models to assess potential risk factors for in-hospital mortality.

Findings: From March 10th to April 15th, 2020, 607 patients were included. Median age was 69 years [interquartile range, {IQR} 22; 65% male). The most common comorbidities were hypertension (276 [46·94%]), diabetes (95 [16·16%]), chronic cardiac (133 [22·62%]) and respiratory (114 [19·39%]) diseases. 141 patients (23·2%) died. In the multivariate model the risk of death increased with older age (odds ratio, for every year of age, 1·15, [95% CI 1·11 - 1·2]), tocilizumab therapy (2·4, [1·13 - 5·11]), C-reactive protein at admission (1·07, per 10 mg/L, [1·04 - 1·10]), d-dimer > 2·5 μg/mL (1·99, [1·03 - 3·86]), diabetes mellitus (2·61, [1·19 - 5·73]), and the PaO2/FiO2 at admission (0·99, per every 1 mmHg, [0·98 - 0·99]). Among the prescribed therapies (tocilizumab, glucocorticoids, lopinavir/ritonavir, hydroxychloroquine, cyclosporine), only cyclosporine was associated with a significant decrease in mortality (0·24, [0·12 - 0·46]; p<0·001).

Interpretation: In a real-clinical setting, inhibition of the calcineurin inflammatory pathway, NF-κB, could reduce the hyperinflammatory phase in COVID-19. The findings might entail relevant implications for the therapy of this disease and could boost the design of new clinical trials among subjects affected by severe COVID-19.

Reference

https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(20)30335-7/fulltext

Safety and immunogenicity of an inactivated SARS-CoV-2 vaccine, BBIBP-CorV: A randomised, double-blind, placebo-controlled, phase 1/2 trial

Abstract

Background: The ongoing COVID-19 pandemic warrants accelerated efforts to test vaccine candidates. It was aimed to assess the safety and immunogenicity of an inactivated severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine candidate, BBIBP-CorV, in humans.

Methods: A randomised, double-blind, placebo-controlled, phase 1/2 trial was done at Shangqiu City Liangyuan District Center for Disease Control and Prevention in Henan Province, China. In phase 1, healthy people aged 18–80 years, who were negative for serum-specific IgM/IgG antibodies against SARS-CoV-2 at the time of screening, were separated into two age groups (18–59 years and ≥60 years) and randomly assigned to receive vaccine or placebo in a two-dose schedule of 2 μg, 4 μg, or 8 μg on days 0 and 28. In phase 2, healthy adults (aged 18–59 years) were randomly assigned (1:1:1:1) to receive vaccine or placebo on a single-dose schedule of 8 μg on day 0 or on a two-dose schedule of 4 μg on days 0 and 14, 0 and 21, or 0 and 28. Participants within each cohort were randomly assigned by stratified block randomisation (block size eight) and allocated (3:1) to receive vaccine or placebo. Group allocation was concealed from participants, investigators, and outcome assessors. The primary outcomes were safety and tolerability. The secondary outcome was immunogenicity, assessed as the neutralising antibody responses against infectious SARS-CoV-2. This study is registered with www.chictr.org.cn, ChiCTR2000032459.

Findings: In phase 1, 192 participants were enrolled (mean age 53·7 years [SD 15·6]) and were randomly assigned to receive vaccine (2 μg [n=24], 4 μg [n=24], or 8 μg [n=24] for both age groups [18–59 years and ≥60 years]) or placebo (n=24). At least one adverse reaction was reported within the first 7 days of inoculation in 42 (29%) of 144 vaccine recipients. The most common systematic adverse reaction was fever (18–59 years, one [4%] in the 2 μg group, one [4%] in the 4 μg group, and two [8%] in the 8 μg group; ≥60 years, one [4%] in the 8 μg group). All adverse reactions were mild or moderate in severity. No serious adverse event was reported within 28 days post vaccination. Neutralising antibody geometric mean titres were higher at day 42 in the group aged 18–59 years (87·7 [95% CI 64·9–118·6], 2 μg group; 211·2 [158·9–280·6], 4 μg group; and 228·7 [186·1–281·1], 8 μg group) and the group aged 60 years and older (80·7 [65·4–99·6], 2 μg group; 131·5 [108·2–159·7], 4 μg group; and 170·87 [133·0–219·5], 8 μg group) compared with the placebo group (2·0 [2·0–2·0]). In phase 2, 448 participants were enrolled (mean age 41·7 years [SD 9·9]) and were randomly assigned to receive the vaccine (8 μg on day 0 [n=84] or 4 μg on days 0 and 14 [n=84], days 0 and 21 [n=84], or days 0 and 28 [n=84]) or placebo on the same schedules (n=112). At least one adverse reaction within the first 7 days was reported in 76 (23%)

of 336 vaccine recipients (33 [39%], 8 μg day 0; 18 [21%], 4 μg days 0 and 14; 15 [18%], 4 μg days 0 and 21; and ten [12%], 4 μg days 0 and 28). One placebo recipient in the 4 μg days 0 and 21 group reported grade 3 fever, but was self-limited and recovered. All other adverse reactions were mild or moderate in severity. The most common systematic adverse reaction was fever (one [1%], 8 μg day 0; one [1%], 4 μg days 0 and 14; three [4%], 4 μg days 0 and 21; two [2%], 4 μg days 0 and 28). The vaccine-elicited neutralising antibody titres on day 28 were significantly greater in the 4 μg days 0 and 14 (169·5, 95% CI 132·2–217·1), days 0 and 21 (282·7, 221·2–361·4), and days 0 and 28 (218·0, 181·8–261·3) schedules than the 8 μg day 0 schedule (14·7, 11·6–18·8; all p<0·001).

Interpretation: The inactivated SARS-CoV-2 vaccine, BBIBP-CorV, is safe and well tolerated at all tested doses in two age groups. Humoral responses against SARS-CoV-2 were induced in all vaccine recipients on day 42. Two-dose immunisation with 4 μg vaccine on days 0 and 21 or days 0 and 28 achieved higher neutralising antibody titres than the single 8 μg dose or 4 μg dose on days 0 and 14.

Reference

https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30831-8/fulltext

Comparative host-coronavirus protein interaction networks reveal pan-viral disease mechanisms

Abstract

The COVID-19 (Coronavirus disease-2019) pandemic, caused by the SARS-CoV-2 coronavirus, is a significant threat to public health and the global economy. SARS-CoV-2 is closely related to the more lethal but less transmissible coronaviruses SARS-CoV-1 and MERS-CoV. Here, comparative viral-human protein-protein interaction and viral protein localization analysis for all three viruses, was carried out. Subsequent functional genetic screening identified host factors that functionally impinge on coronavirus proliferation, including Tom70, a mitochondrial chaperone protein that interacts with both SARS-CoV-1 and SARS-CoV-2 Orf9b, an interaction was structurally characterized using cryo-EM. Combining genetically-validated host factors with both COVID-19 patient genetic data and medical billing records identified important

molecular mechanisms and potential drug treatments that merit further molecular and clinical study.

Reference

https://science.sciencemag.org/content/early/2020/10/14/science.abe9403

NEWS LETTER

Publication Date: Oct 19, 2020

Could certain COVID-19 vaccines leave people more vulnerable to the AIDS virus?

Certain COVID-19 vaccine candidates could increase susceptibility to HIV, warns a group of researchers who in 2007 learned that an experimental HIV vaccine had raised in some people the risk for infection with the AIDS virus. These concerns have percolated in the background of the race for a vaccine to stem the coronavirus pandemic, but now the researchers have gone public with a “cautionary tale,” in part because trials of those candidates may soon begin in locales that have pronounced HIV epidemics, such as South Africa.

Some approved and experimental vaccines have as a backbone a variety of adenoviruses, which can cause the common cold but are often harmless. The ill-fated HIV vaccine trial used an engineered strain known as adenovirus 5 (Ad5) to shuttle into the body the gene for the surface protein of the AIDS virus. In four candidate COVID-19 vaccines now in clinical trials in several countries, including the United States, Ad5 similarly serves as the “vector” to carry in the surface protein gene of SARS-CoV-2, the viral cause of the pandemic; two of these have advanced to large-scale, phase III efficacy studies in Russia and Pakistan. For more details, read the link given below.

Reference

https://www.sciencemag.org/news/2020/10/could-certain-covid-19-vaccines-leave-people-more-vulnerable-aids-virus

CORRESPONDANCE

Publication Date: Oct 19, 2020

GeneXpert for the diagnosis of COVID-19 in LMICs

Abstract

Since the emergence of the COVID-19 pandemic, caused by infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), most countries were struggling with early detection of SARS-CoV-2 and subsequent rapid case management and contact tracing. Inadequate access to diagnostic testing and health-care facilities, which is particularly pronounced in resource-poor settings such as Madagascar, is substantially impeding COVID-19 control efforts. In this low-income country, approximately 12 million people (over half of the population) live in rural areas with poor access to primary health services and even less access to specific diagnostic services, such as SARS-CoV-2 testing. Only 60–70% of people living in Madagascar have access to any health facilities. There are 1·6 physicians per 10 000 individuals and diagnostic laboratories are scarce and under-equipped; therefore, many patients have inaccurate diagnoses and, in some cases, inappropriate treatment.

In 2012, the GeneXpert MTB/RIF molecular platform (Xpert; Cepheid, Sunnyvale, CA, USA) was used in Madagascar to upscale the capacity for tuberculosis diagnostic testing. In response to the COVID-19 pandemic, multiple RT-PCR assays, including the Cepheid Xpert Xpress SARS-CoV-2, have received authorisation for emergency use from the US Food and Drug Administration. This 50 min RT-PCR-based assay detects the pan-sarbecovirus *E* gene and the N2 region of the *N* gene as its SARS-CoV-2-specific target. For more details, read the link give below.

Reference

https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(20)30428-9/fulltext

Scientific consensus on the COVID-19 pandemic: We need to act now

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has infected more than 35 million people globally, with more than 1 million deaths recorded by WHO as of Oct 12, 2020. As a second wave of COVID-19 affects Europe, and with winter approaching, we need clear communication about the risks posed by COVID-19 and effective strategies to combat them. Here, we share our view of the current evidence-based consensus on COVID-19.

SARS-CoV-2 spreads through contact (via larger droplets and aerosols), and longer-range transmission via aerosols, especially in conditions where ventilation is poor. Its high infectivity, combined with the susceptibility of unexposed populations to a new virus, creates conditions for rapid community spread. The infection fatality rate of COVID-19 is several-fold higher than that of seasonal influenza, and infection can lead to persisting illness, including in young, previously healthy people (ie, long COVID). It is unclear how long protective immunity lasts, and, like other seasonal coronaviruses, SARS-CoV-2 is capable of re-infecting people who have already had the disease, but the frequency of re-infection is unknown. Transmission of the virus can be mitigated through physical distancing, use of face coverings, hand and respiratory hygiene, and by avoiding crowds and poorly ventilated spaces. Rapid testing, contact tracing, and isolation are also critical to controlling transmission. WHO has been advocating for these measures since early in the pandemic.

Reference

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32153-X/fulltext

PERSPECTIVE

Publication Date: Oct 21, 2020

Understanding COVID-19 vaccine efficacy

The elderly and people with comorbidities are at greatest risk of severe coronavirus disease 2019 (COVID-19). A safe and effective vaccine could help to protect these groups in two distinct ways: direct protection, where high-risk groups are vaccinated to prevent disease, and indirect protection, where those in contact with high-risk individuals are vaccinated to reduce transmission. Influenza vaccine campaigns initially targeted the elderly, in an effort at direct protection, but more recently have focused on the general population, in part to enhance indirect protection. Because influenza vaccines induce weaker, shorter-lived immune responses in the elderly than in young adults, increasing indirect protection may be a more effective strategy. It is unknown whether the same is true for COVID-19 vaccines. For COVID-19, age-structured mathematical models with realistic contact patterns are being used to explore different vaccination plans, with the recognition that vaccine doses may be limited at first and so should be deployed strategically. But as supplies grow large enough to contemplate an indirect protection strategy, the recommendations of these models depend on the details of how, and how well, these vaccines work and in which groups of people. For more details, read the link given below.

Reference

https://science.sciencemag.org/content/early/2020/10/21/science.abe5938

Publication Date: Oct 16, 2020

COVID-19 in children and young people

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has brought distinct challenges to the care of children and adolescents globally. Unusually for a respiratory viral infection, children and adolescents are at much lower risk from symptomatic coronavirus disease 2019 (COVID-19) than any other age group. The

near-global closure of schools in response to the pandemic reflected the reasonable expectation from previous respiratory virus outbreaks that children would be a key component of the transmission chain. However, emerging evidence suggests that this is most likely not the case. A minority of children experience a postinfectious inflammatory syndrome, the pathology and long-term outcomes of which are poorly understood. However, relative to their risk of contracting disease, children and adolescents have been disproportionately affected by lockdown measures, and advocates of child health need to ensure that children's rights to health and social care, mental health support, and education are protected throughout subsequent pandemic waves.

Evidence from contact-tracing studies suggest that children and teenagers are less susceptible to SARS-CoV-2 infection than adults; however, community swabbing and seroprevalence studies conducted outside of outbreak settings suggest that infection rates are similar to those in older age groups. Only half of children and teenagers with antibodies against SARS-CoV-2 have experienced symptoms, and there is growing evidence that there is a broad range of presentations, emphasizing the limitations of community-based prevalence studies based on testing only children with respiratory symptoms. Hospitalization for severe acute COVID-19 in children is rare, but among these pediatric inpatients, respiratory symptoms are more apparent than in infected children in the community. Case fatality in hospitalized children is, fortunately, relatively low at 1% (compared with 27% across all ages).

The reason for the lower burden of symptomatic disease in children is not yet clear. Upper airway expression of angiotensin-converting enzyme 2 (ACE2), a receptor for the SARS-CoV-2 spike protein, increases with age, and higher ACE2 expression correlates with being positive for SARS-CoV-2 genomic RNA in swabs of upper respiratory tracts from symptomatic children, but not with viral load. An alternative proposal is the absence in children of maladaptive immune responses that lead to acute respiratory distress syndrome (ARDS) in older age groups, but there are likely other unidentified mechanisms.

Reference

https://science.sciencemag.org/content/370/6514/286

IN DEPTH

Publication Date: Oct 16, 2020

Found: Genes that sway the course of the coronavirus

Most people infected by SARS-CoV-2 never feel sick, whereas others develop serious symptoms or even end up in an intensive care unit clinging to life. Age and preexisting conditions, such as obesity, account for much of the disparity. But geneticists have raced to see whether a person's DNA also explains why some get hit hard by the coronavirus, and they have uncovered tantalizing leads. A U.K. group studying more than 2200 COVID-19 patients has pinned down common gene variants that are linked to the most severe cases of the disease, and that point to existing drugs that could be repurposed to help.

The new study confirmed the chromosome 3 region's involvement. And because 74% of its patients were so sick that they needed invasive ventilation, it had the statistical strength to reveal other markers, elsewhere in the genome, linked to severe COVID-19. One find is a gene called IFNAR2 that codes for a cell receptor for interferon, a powerful molecular messenger that rallies the immune defenses when a virus invades a cell. A variant of IFNAR2 found in one in four Europeans raised the risk of severe COVID-19 by 30%. Baillie says the IFNAR2 hit is “entirely complementary” to a finding reported in Science last month: Very rare mutations that disable IFNAR2 and seven other interferon genes may explain about 4% of severe COVID-19 cases (25 September, p. 1550). Both studies raise hopes for ongoing trials of interferons as a COVID-19 treatment. For more details, read the link given below.

Reference

https://science.sciencemag.org/content/370/6514/275

REPORT

Publication Date: Oct 20, 2020

Structural analysis of full-length SARS-CoV-2 spike protein from an advanced vaccine candidate

Vaccine efforts against the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) responsible for the current COVID-19 pandemic are focused on SARS-CoV-2 spike glycoprotein, the primary target for neutralizing antibodies. A cryo-EM and site-specific glycan analysis was performed of one of the leading subunit vaccine candidates from Novavax based on a full-length spike protein formulated in polysorbate 80 (PS 80) detergent. The studies revealed a stable prefusion conformation of the spike immunogen with slight differences in the S1 subunit compared to published spike ectodomain structures. Novel interactions between the spike trimers was also observed, allowing formation of higher order spike complexes. This study confirms the structural integrity of the full-length spike protein immunogen and provides a basis for interpreting immune responses to this multivalent nanoparticle immunogen.

Reference

https://science.sciencemag.org/content/early/2020/10/19/science.abe1502

Neuropilin-1 is a host factor for SARS-CoV-2 infection

SARS-CoV-2, the causative agent of COVID-19, uses the viral Spike (S) protein for host cell attachment and entry. The host protease furin cleaves the full-length precursor S glycoprotein into two associated polypeptides: S1 and S2. Cleavage of S generates a polybasic Arg-Arg-Ala-Arg C-terminal sequence on S1, which conforms to a C-end rule (CendR) motif that binds to cell surface Neuropilin-1 (NRP1) and Neuropilin-2 (NRP2) receptors. Here, we used X-ray crystallography and biochemical approaches to show that the S1 CendR motif directly bound NRP1. Blocking this interaction using RNAi or selective inhibitors reduced SARS-CoV-2 entry and infectivity in cell culture. NRP1 thus serves as a host factor for SARS-CoV-2 infection and may potentially provide a therapeutic target for COVID-19.

Reference

https://science.sciencemag.org/content/early/2020/10/19/science.abd3072

Neuropilin-1 facilitates SARS-CoV-2 cell entry and infectivity

The causative agent of coronavirus induced disease 2019 (COVID-19) is the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). For many viruses, tissue tropism is determined by the availability of virus receptors and entry cofactors on the surface of host cells. Here, it was found that neuropilin-1 (NRP1), known to bind furin-cleaved substrates, significantly potentiates SARS-CoV-2 infectivity, an effect blocked by a monoclonal blocking antibody against NRP1. A SARS-CoV-2 mutant with an altered furin cleavage site did not depend on NRP1 for infectivity. Pathological analysis of human COVID-19 autopsies revealed SARS-CoV-2 infected cells including olfactory neuronal cells facing the nasal cavity positive for NRP1. The data provide insight into SARS-CoV-2 cell infectivity and define a potential target for antiviral intervention.

Reference

https://science.sciencemag.org/content/early/2020/10/19/science.abd2985

REPORT

Publication Date: Oct 15, 2020

A promising inactivated whole-virion SARS-CoV-2 vaccine

The ongoing COVID-19 pandemic is the only outbreak to date in which the time from identification of a pathogen to the presentation of the first clinical trial results for a specific vaccine against the pathogen was less than 9 months. By September, 2020, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine landscape included 39 candidates being tested in clinical trials and more than 200 candidates in preclinical development. It is generally accepted that only vaccines can halt the spread of the pandemic virus; thus, several groups have already published interim results of phase 1/2 clinical trials of SARS-CoV-2 vaccines generated on various vaccine platforms. It is critical to accumulate as many clinical data on the safety and immunogenicity of SARS-CoV-2 vaccines as possible, because this infection is new to the human population and all possible short-term or long-term rare adverse events are difficult to predict. In this regard, the study by Shengli Xia and colleagues is timely because it provides valuable evidence for the safety and immunogenicity of a β-propiolactone inactivated aluminium hydroxide-adjuvanted whole-virion SARS-CoV-2 vaccine candidate developed by China National Biotec Group and the Beijing Institute of Biological Products (BBIBP-CorV), which was tested in randomised, double-blind, placebo-controlled phase 1/2 clinical trials in healthy individuals aged 18 years and older.

Importantly, this was the first study of an inactivated SARS-CoV-2 vaccine to include participants older than 60 years—the most vulnerable age group for this infection. In the phase 1 dose-escalating trial, the vaccine was given at a two-dose schedule at three different concentrations (2 μg, 4 μg, and 8 μg per dose) and was well tolerated in both age groups (18–59 years and ≥60 years). The older age group had lower rates of solicited adverse events than the younger adults: the overall rates of adverse events within 28 days after vaccination were 34 (47%) of 72 participants in the group aged 18–59 years, compared with 14 (19%) of 72 participants in the group aged 60 years and older. At the same time, in both age groups the vaccine was similarly immunogenic: the

geometric mean anti-SARS-CoV-2 neutralising antibody titres measured by a 50% virus neutralisation assay 14 days after the booster dose were 88, 211, and 229 in the group aged 18–59 years and 81, 132, and 171 in the group aged 60 years and older for 2 µg, 4 µg, and 8 µg vaccine doses, respectively. Moreover, the authors tested cross-reactivity of the neutralising antibodies against several drifted SARS-CoV-2 isolates and showed the potential of their vaccine to protect against evolutionary diverged viruses, should they appear in circulation.

Reference

https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30832-X/fulltext