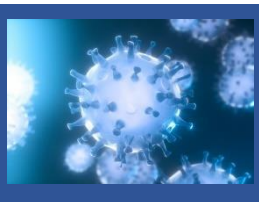
# COVID-19

***Oct 01 - 07, 2020***



# RESEARCH PUBLICATIONS

**Publication Date: Oct 07, 2020**

## Large-scale multi-omic analysis of COVID-19 severity


### Abstract

RNA-Seq and high-resolution mass spectrometry was performed on 128 blood samples from COVID-19 positive and negative patients with diverse disease severities and outcomes. Quantified transcripts, proteins, metabolites, and lipids were associated with clinical outcomes in a curated relational database, uniquely enabling systems analysis and cross-ome correlations to molecules and patient prognoses. 219 Molecular features were maped with high significance to COVID-19 status and severity, many involved in complement activation, dysregulated lipid transport, and neutrophil activation. Sets of covarying molecules were identified, *e.g.*, protein gelsolin and metabolite citrate or plasmalogens and apolipoproteins, offering pathophysiological insights and therapeutic suggestions. The observed dysregulation of platelet function, blood coagulation, acute phase response, and endotheliopathy further illuminated the unique COVID-19 phenotype. We present a web-based tool (covid-omics.app) enabling interactive exploration of our compendium and illustrate its utility through a machine learning approach for prediction of COVID-19 severity.


### Reference


https://www.cell.com/cell-systems/fulltext/S2405-4712(20)30371-9

## COVID-19-induced ARDS is associated with decreased frequency of activated memory/effector T cells expressing tissue migration molecule CD11a++


### Abstract

Preventing the progression to acute respiratory distress syndrome (ARDS) in COVID-19 is an unsolved challenge. The involvement of T cell immunity in this exacerbation remains unclear. To identify predictive markers of COVID-19 progress and outcome, we analyzed peripheral blood of 10 COVID-19-associated ARDS patients and 35 mild/moderate COVID-19 patients, not requiring intensive care. Using multi-parametric flow cytometry, we compared quantitative, phenotypic and functional characteristics of circulating bulk immune cells, and SARS-CoV-2 S-protein reactive T cell between the two groups. ARDS patients demonstrated significantly higher S-protein reactive CD4+ and CD8+ T cells compared to non-ARDS patients. Of interest, comparison of circulating bulk T cells in ARDS patients to non-ARDS patients demonstrated decreased frequencies of CD4+ and CD8+ T cell subsets with activated memory/effector T cells expressing tissue migration molecule CD11a++. Importantly, survival from ARDS (4/10) was accompanied by a recovery of the CD11a++ T cell subsets in peripheral blood. Conclusively, data on S-protein reactive polyfunctional T cells indicate the ability of ARDS patients to generate antiviral protection. Furthermore, decreased frequencies of activated memory/effector T cells expressing tissue migratory molecule CD11a++ observed in circulation of ARDS patients might suggest their involvement in ARDS development and propose CD11a-based immune signature as a possible prognostic marker.


### Reference


https://www.cell.com/molecular-therapy-family/molecular-therapy/fulltext/S1525-0016(20)30535-9

## Crystallographic and electrophilic fragment screening of the SARS-CoV-2 main protease


### Abstract

COVID-19, caused by SARS-CoV-2, lacks effective therapeutics. Additionally, no antiviral drugs or vaccines were developed against the closely related coronavirus, SARS-CoV-1 or MERS-CoV, despite previous zoonotic outbreaks. To identify starting points for such therapeutics, we performed a large-scale screen of electrophile and non-covalent fragments through a combined mass spectrometry and X-ray approach against the SARS-CoV-2 main protease, one of two cysteine viral proteases essential for viral replication. Our crystallographic screen identified 71 hits that span the entire active site, as well as 3 hits at the dimer interface. These structures reveal routes to rapidly develop more potent inhibitors through merging of covalent and non-covalent fragment hits; one series of low-reactivity, tractable covalent fragments were progressed to discover improved binders. These combined hits offer unprecedented structural and reactivity information for on-going structure-based drug design against SARS-CoV-2 main protease.


### Reference


https://www.nature.com/articles/s41467-020-18709-w


## Metallodrug ranitidine bismuth citrate suppresses SARS-CoV-2 replication and relieves virus-associated pneumonia in Syrian hamsters


### Abstract

SARS-CoV-2 is causing a pandemic of COVID-19, with high infectivity and significant mortality1. Currently, therapeutic options for COVID-19 are limited. Historically, metal compounds have found use as antimicrobial agents, but their antiviral activities have rarely been explored. Here, a set of metallodrugs and related compounds were tested, and identify ranitidine bismuth citrate, a commonly used drug for the treatment of *Helicobacter pylori* infection, as a potent anti-SARS-CoV-2 agent, both *in vitro* and *in vivo*. Ranitidine bismuth citrate exhibited low cytotoxicity and protected SARS-CoV-2-infected cells with a high selectivity index of 975. Importantly, ranitidine bismuth citrate

suppressed SARS-CoV-2 replication, leading to decreased viral loads in both upper and lower respiratory tracts, and relieved virus-associated pneumonia in a golden Syrian hamster model. In vitro studies showed that ranitidine bismuth citrate and its related compounds exhibited inhibition towards both the ATPase (IC50 = 0.69 μM) and DNA-unwinding (IC50 = 0.70 μM) activities of the SARS-CoV-2 helicase via an irreversible displacement of zinc(II) ions from the enzyme by bismuth(III) ions. Our findings highlight viral helicase as a druggable target and the clinical potential of bismuth(III) drugs or other metallodrugs for the treatment of SARS-CoV-2 infection.

**Reference**

https://www.nature.com/articles/s41564-020-00802-x

## A novel severity score to predict inpatient mortality in COVID-19 patients

**Abstract**

COVID-19 is commonly mild and self-limiting, but in a considerable portion of patients the disease is severe and fatal. Determining which patients are at high risk of severe illness or mortality is essential for appropriate clinical decision making. A novel severity score specifically for COVID-19 was proposed to help predict disease severity and mortality. 4711 patients with confirmed SARS-CoV-2 infection were included. A risk model was derived using the first half of the cohort (n = 2355 patients) by logistic regression and bootstrapping methods. The discriminative power of the risk model was assessed by calculating the area under the receiver operating characteristic curves (AUC). The severity score was validated in a second half of 2356 patients. Mortality incidence was 26.4% in the derivation cohort and 22.4% in the validation cohort. A COVID-19 severity score ranging from 0 to 10, consisting of age, oxygen saturation, mean arterial pressure, blood urea nitrogen, C-Reactive protein, and the international normalized ratio was developed. A ROC curve analysis was performed in the derivation cohort achieved an AUC of 0.824 (95% CI 0.814–0.851) and an AUC of 0.798 (95% CI 0.789–0.818) in the validation cohort. Furthermore, based on the risk categorization the probability of mortality was 11.8%, 39% and 78% for patient with low (0–3), moderate (4–6) and high (7–10) COVID-19 severity score. This developed and validated novel COVID-19 severity score will aid physicians in predicting mortality during surge periods.

**Reference**

https://www.nature.com/articles/s41598-020-73962-9

## Extrafollicular B cell responses correlate with neutralizing antibodies and morbidity in COVID-19

**Abstract**

A wide spectrum of clinical manifestations has become a hallmark of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) COVID-19 pandemic, although the immunological underpinnings of diverse disease outcomes remain to be defined. A detailed characterization of B cell responses was performed through high-dimensional flow cytometry to reveal substantial heterogeneity in both effector and immature populations. More notably, critically ill patients displayed hallmarks of extrafollicular B cell activation and shared B cell repertoire features previously described in autoimmune settings. Extrafollicular activation correlated strongly with large antibody-secreting cell expansion and early production of high concentrations of SARS-CoV-2-specific neutralizing antibodies. Yet, these patients had severe disease with elevated inflammatory biomarkers, multiorgan failure and death. Overall, these findings strongly suggest a pathogenic role for immune activation in subsets of patients with COVID-19. Our study provides further evidence that targeted immunomodulatory therapy may be beneficial in specific patient subpopulations and can be informed by careful immune profiling.

**Reference**

https://www.nature.com/articles/s41590-020-00814-z

## A novel severity score to predict inpatient mortality in COVID-19 patients

**Abstract**

COVID-19 is commonly mild and self-limiting, but in a considerable portion of patients the disease is severe and fatal. Determining which patients are at high risk of severe illness or mortality is essential for appropriate clinical decision making. A novel severity score was proposed specifically for COVID-19 to help predict disease severity and

mortality. 4711 patients with confirmed SARS-CoV-2 infection were included. A risk model was derived using the first half of the cohort (n = 2355 patients) by logistic regression and bootstrapping methods. The discriminative power of the risk model was assessed by calculating the area under the receiver operating characteristic curves (AUC). The severity score was validated in a second half of 2356 patients. Mortality incidence was 26.4% in the derivation cohort and 22.4% in the validation cohort. A COVID-19 severity score ranging from 0 to 10, consisting of age, oxygen saturation, mean arterial pressure, blood urea nitrogen, C-reactive protein, and the international normalized ratio was developed. A ROC curve analysis was performed in the derivation cohort achieved an AUC of 0.824 (95% CI 0.814–0.851) and an AUC of 0.798 (95% CI 0.789–0.818) in the validation cohort. Furthermore, based on the risk categorization the probability of mortality was 11.8%, 39% and 78% for patient with low (0–3), moderate (4–6) and high (7–10) COVID-19 severity score. This developed and validated novel COVID-19 severity score will aid physicians in predicting mortality during surge periods.

**Reference**

https://www.nature.com/articles/s41598-020-73962-9

**Publication Date: Oct 06, 2020**

## Main protease of SARS-CoV-2 serves as a bifunctional molecule in restricting type I interferon antiviral signaling

**Abstract**

At present, the world is suffering from an ongoing pandemic of 2019 novel coronavirus (COVID-19) which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2/2019-nCoV). To date, >20 million cases were confirmed with a death toll at >700,000. Although there are no clinically specific and effective antiviral treatments toward SARS-CoV-2 infection so far, the pathological study of SARS-CoV-2 infection and the development of SARS-CoV-2-specific vaccines are progressing rapidly within these several months. However, few reports mentioned the mechanism employed by SARS-CoV-2 for evading from surveillance of immune system.

During viral infection, type I interferon (IFN) responses serve as the first defensive line against invading viruses by inducing a group of antiviral interferon-stimulated genes (ISGs). Previous studies showed that early and proper type I IFN production could induce antiviral responses and potentiate the adaptive immune, thus effectively limiting coronavirus infection, including SARS-CoV-2. It has been reported that SARS-CoV-2 fails to induce robust IFN signaling, and impaired IFN responses was observed in patients with severe SARS-CoV-2 infection, suggesting that SARS-CoV-2 might develop multiple strategies to limit competent IFN production. To investigate the influence of SARS-CoV-2 on type I IFN signaling during infection, Huh7 cells and Calu3 cells were infected with SARS-CoV-2. SARS-CoV-2 infection induced type I IFN activation and enhanced the phosphorylation level of TANK-binding kinase 1 (TBK1) and IFN regulatory factor 3 (IRF3), leading to the induction of retinoic acid-inducible gene I (RIG-I), the major viral RNA sensor in the cytosol. It was further confirmed that RIG-I is required for IFNB induction by SARS-CoV-2 infection. Although IFNβ pretreatment was shown to reduce the replication of SARS-CoV-2 effectively as previously reported, SARS-CoV-2-induced IFNβ signaling was relatively low, suggesting that SARS-CoV-2 inhibited type I IFN production. We next ectopically expressed different SARS-CoV-2 proteins to study their roles in type I IFN signaling. Among them, SARS-CoV-2 main protease (Mpro, also called 3CLpro or nsp5) was proved to be a potent inhibitor of type I IFN signaling. To confirm whether Mpro inhibits viral RNA-induced IFN signaling, we treated the Mpro-transfected cells with intracellular poly(I:C) and found that Mpro reduced IFNβ signaling activation. As IFNβ induction requires coordination between IRF3- and nuclear factor (NF)-κB-mediated signaling pathways, we sought to determine the inhibition of Mpro in both IRF3-mediated and NF-κB pathway using IFN-stimulated response element (ISRE, which only needs IRF3 activation) and NF-κB luciferase reporters separately. Mpro was shown to inhibit both ISRE- and NF-κB-mediated signaling while the regulatory roles of Mpro in type I IFN pathway were relatively stronger. Consistently, overexpression of Mpro could restrain the phosphorylation of TBK1 and IRF3 after Sendai virus infection. We then found that Mpro decreased the IFNβ luciferase reporter activity induced by the active mutant of RIG-I [RIG-I (2CARD)] but not the downstream signaling proteins such as mitochondrial antiviral signaling protein, TBK1, or the active form of IRF3 [IRF3(5D)]. In addition, co-immunoprecipitation analysis showed that Mpro could interact with RIG-I but not the

downstream signaling proteins, indicating that Mpro might target RIG-I. After recognizing viral RNAs, RIG-I undergoes K63-linked poly-ubiquitination mediated by TRIM25 to turn into its activated form by releasing its CARD domains. We next investigated whether Mpro affects the K63-linked ubiquitination of RIG-I as well as its association with its E3 ligase TRIM25.4 We found that overexpression of Mpro reduced the K63-linked ubiquitination of RIG-I as well as the interaction between RIG-I and TRIM25 after viral infection. Taken together, these data revealed that SARS-CoV-2 Mpro might restrict IFN induction by reducing K63-linked ubiquitination on RIG-I. It remains elusive whether SARS-CoV-2 uses different strategies to suppress IFN signaling to improve its infectious ability, compared with SARS-CoV, another highly related pathogenic coronavirus. To investigate the differences between the Mpro of SARS-CoV-2 and SARS-CoV, we compared the function of Mpro from these two coronaviruses in regulating IFN signaling and found that Mpro of both coronaviruses could inhibit the IFN induction, while SARS-CoV-2 Mpro showed a relatively higher inhibitory activity than SARS-CoV Mpro. The stronger IFN antagonism of SARS-CoV-2 Mpro might further reduce antiviral responses in infected cells and thus enhancing SARS-CoV-2 incubation period and viral replication during infection. For more details, read the link given below.

**Reference**

https://www.nature.com/articles/s41392-020-00332-2

## Salvianolic acid C potently inhibits SARS-CoV-2 infection by blocking the formation of six-helix bundle core of spike protein

**Abstract**

The pandemic of COVID-19 caused by SARS-CoV-2 infection has posed a serious threat to global public health and the economy. Up to now, although several potentially effective antiviral drugs are under evaluating in clinical trials around the world, there are still no specific antiviral countermeasures beyond supportive therapies have been established. We herein report that the hydrophilic compound Salvianolic acid C (Sal-C) from Danshen, a traditional Chinese medicine (TCM), potently inhibit SARS-CoV-2 infection by blocking the formation of six-helix bundle (6-HB) core of spike (S) protein.

The spike protein of SARS-CoV-2 plays a key role in receptor recognition and virus-cell membrane fusion and shows a great efficiency in mediating virus entry, which is consisted of S1 and S2 subunits. After binding to the cell receptor via receptor-binding domain (RBD) in S1, SARS-CoV-2 S2 will change its conformation by forming a 6-HB between HR1 and HR2 (two main components of S2 subunits) domains, leading to viral membrane fusion.2 In view of the high transmission rate and infection rate of SARS-CoV-2, we focused on the S2 subunit with highly conservative properties as a target to develop small-molecule inhibitors for SARS-CoV-2 S-mediated cell–cell fusion.

Based on our previous studies on seeking for h-CoVs fusion inhibitors, we utilized the cell–cell fusion assay mediated by SARS-CoV-2 S protein to screen the TCM monomer library for discovering fusion inhibitors. And, Sal-C was identified to potently inhibit the membrane fusion of S-overexpressed-HEK293T and Vero-E6 cells with half maximal inhibitory concentration ($IC_{50}$) of 1.71 μM. For more details, read the link given below.

**Reference**

https://www.nature.com/articles/s41392-020-00325-1

## A simple RNA preparation method for SARS-CoV-2 detection by RT-qPCR

**Abstract**

The technique RT-qPCR for viral RNA detection is the current worldwide strategy used for early detection of the novel coronavirus SARS-CoV-2. RNA extraction is a key pre-analytical step in RT-qPCR, often achieved using commercial kits. However, the magnitude of the COVID-19 pandemic is causing disruptions to the global supply chains used by many diagnostic laboratories to procure the commercial kits required for RNA extraction. Shortage in these essential reagents is even more acute in developing countries with no means to produce kits locally. It was sought to find an alternative procedure to replace commercial kits using common reagents found in molecular biology laboratories. Here we report a method for RNA extraction that takes about 40 min to complete ten samples, and is not more laborious than current commercial RNA extraction kits. It was demonstrated that this method can be used to process nasopharyngeal swab samples and yields RT-qPCR results comparable to those obtained with commercial kits. Most importantly, this procedure can be easily

implemented in any molecular diagnostic laboratory. Frequent testing is crucial for individual patient management as well as for public health decision making in this pandemic. Implementation of this method could maintain crucial testing going despite commercial kit shortages.

**Reference**

https://www.nature.com/articles/s41598-020-73616-w

## Risk estimation of SARS-CoV-2 transmission from bluetooth low energy measurements

**Abstract**

Digital contact tracing approaches based on Bluetooth low energy (BLE) have the potential to efficiently contain and delay outbreaks of infectious diseases such as the ongoing SARS-CoV-2 pandemic. In this work, a machine learning based approach was proposed to reliably detect subjects that have spent enough time in close proximity to be at risk of being infected. This study is an important proof of concept that will aid the battery of epidemiological policies aiming to slow down the rapid spread of COVID-19.

**Reference**

https://www.nature.com/articles/s41746-020-00340-0

## Molecular epidemiology of the first wave of severe acute respiratory syndrome coronavirus 2 infection in Thailand in 2020

**Abstract**

The coronavirus disease 2019 pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a major global concern. Several SARS-CoV-2 gene mutations have been reported. In the current study, associations between SARS-CoV-2 gene variation and exposure history during the first wave of the outbreak in Thailand between January and May 2020 were investigated. Forty samples were collected at different time points during the outbreak, and parts of the SARS-CoV-2 genome sequence were used to assess genomic variation patterns. The phylogenetics of the 40 samples were clustered into L, GH, GR, O and T types. T types were predominant in

Bangkok during the first local outbreak centered at a boxing stadium and entertainment venues in March 2020. Imported cases were infected with various types, including L, GH, GR and O. In southern Thailand introductions of different genotypes were identified at different times. No clinical parameters were significantly associated with differences in genotype. The results indicated local transmission (type T, Spike protein (A829T)) and imported cases (types L, GH, GR and O) during the first wave in Thailand. Genetic and epidemiological data may contribute to national policy formulation, transmission tracking and the implementation of measures to control viral spread.

**Reference**

https://www.nature.com/articles/s41598-020-73554-7

## SARS-CoV-2-specific T-cells in unexposed humans: Presence of cross-reactive memory cells does not equal protective immunity

**Abstract**

Using human blood samples obtained from pre-pandemic donors, a recent article by Mateus *et al.* in Science provided new evidence that SARS-CoV-2-reactive T-cells in unexposed donors are indeed HCoV-specific T-cells. The rapid global spread of coronavirus disease 2019 (COVID-19), caused by the newly-emerged coronavirus SARS-CoV-2, has led to millions of infections with substantial morbidity and mortality. Different clinical manifestations of COVID-19 have been observed: asymptomatic infections, mild self-limiting disease, acute respiratory distress syndrome and death. The determinants underlying disease severity currently remain elusive; since severe patients often present with immune hyper-responsiveness, it is speculated that the host' immune response could be a contributing factor to severe disease.

Many studies are dissecting the human immune response to SARS-CoV-2 and several groups have reported marked activation of T-cell subsets in acute COVID-19 patients. The antigen-specific T-cell response has only been analyzed in a handful of papers, all sharing a common feature: although SARS-CoV-2-specific CD4+ and CD8+ T-cells are consistently detected in peripheral blood mononuclear cells (PBMC) obtained from COVID-19 patients, studies also report activation of T-cells in 20–50% of

the people never exposed to SARS-CoV-2. The frequency of these cross-reactive responses in pre-pandemic controls is always low. On average 1% of the CD4+ T-cells from acute COVID-19 patients upregulate activation markers upon peptide pool stimulation. If pre-pandemic donors respond to peptide stimulation, the percentage of responding CD4+ T-cells is always <0.1%. Authors of these papers speculate that these–mainly CD4+–SARS-CoV-2-reactive T-cells are probably induced by past infection with one of the endemic "common cold" coronaviruses (HCoVs), which share at least partial sequence homology with SARS-CoV-2. Experimental evidence for this hypothesis was lacking so far. For more details, read the link given below.

**Reference**

https://www.nature.com/articles/s41392-020-00338-w

## Sofosbuvir terminated RNA is more resistant to SARS-CoV-2 proofreader than RNA terminated by Remdesivir

**Abstract**

SARS-CoV-2 is responsible for COVID-19, resulting in the largest pandemic in over a hundred years. After examining the molecular structures and activities of hepatitis C viral inhibitors and comparing hepatitis C virus and coronavirus replication, we previously postulated that the FDA-approved hepatitis C drug EPCLUSA (Sofosbuvir/Velpatasvir) might inhibit SARS-CoV-2. It was subsequently demonstrated that Sofosbuvir triphosphate is incorporated by the relatively low fidelity SARS-CoV and SARS-CoV-2 RNA-dependent RNA polymerases (RdRps), serving as an immediate polymerase reaction terminator, but not by a host-like high fidelity DNA polymerase. Other investigators have since demonstrated the ability of Sofosbuvir to inhibit SARS-CoV-2 replication in lung and brain cells; additionally, COVID-19 clinical trials with EPCLUSA and with Sofosbuvir plus Daclatasvir have been initiated in several countries. SARS-CoV-2 has an exonuclease-based proofreader to maintain the viral genome integrity. Any effective antiviral targeting the SARS-CoV-2 RdRp must display a certain level of resistance to this proofreading activity. We report here that Sofosbuvir terminated RNA resists removal by the exonuclease to a substantially higher extent than RNA terminated by Remdesivir, another drug being used as a COVID-19

therapeutic. These results offer a molecular basis supporting the current use of Sofosbuvir in combination with other drugs in COVID-19 clinical trials.

**Reference**

https://www.nature.com/articles/s41598-020-73641-9

## SARS-CoV-2 S1 and *N*-based serological assays reveal rapid seroconversion and induction of specific antibody response in COVID-19 patients

**Abstract**

As the Coronavirus Disease 2019 (COVID-19), which is caused by the novel SARS-CoV-2, continues to spread rapidly around the world, there is a need for well validated serological assays that allow the detection of viral specific antibody responses in COVID-19 patients or recovered individuals. In this study, it was established and used multiple indirect Enzyme Linked Immunosorbent Assay (ELISA)-based serological assays to study the antibody response in COVID-19 patients. In order to validate the assays we determined the cut off values, sensitivity and specificity of the assays using sera collected from pre-pandemic healthy controls, COVID-19 patients at different time points after disease-onset, and seropositive sera to other human coronaviruses (CoVs). The developed SARS-CoV-2 S1 subunit of the spike glycoprotein and nucleocapsid (*N*)-based ELISAs not only showed high specificity and sensitivity but also did not show any cross-reactivity with other CoVs. It was also shown that all RT-PCR confirmed COVID-19 patients tested in our study developed both virus specific IgM and IgG antibodies as early as week one after disease onset. Our data also suggest that the inclusion of both S1 and N in serological testing would capture as many potential SARS-CoV-2 positive cases as possible than using any of them alone. This is specifically important for tracing contacts and cases and conducting large-scale epidemiological studies to understand the true extent of virus spread in populations.

**Reference**

https://www.nature.com/articles/s41598-020-73491-5

## Characteristics of SARS-CoV-2 and COVID-19

### Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a highly transmissible and pathogenic coronavirus that emerged in late 2019 and has caused a pandemic of acute respiratory disease, named ‘coronavirus disease 2019’ (COVID-19), which threatens human health and public safety. In this Review, the basic virology of SARS-CoV-2 was described, including genomic characteristics and receptor use, highlighting its key difference from previously known coronaviruses. Current knowledge of clinical, epidemiological and pathological features of COVID-19 was summarized, as well as recent progress in animal models and antiviral treatment approaches for SARS-CoV-2 infection. The potential wildlife hosts and zoonotic origin of this emerging virus was also discussed in detail.

### Reference

https://www.nature.com/articles/s41579-020-00459-7

## The efficacy assessment of convalescent plasma therapy for COVID-19 patients: A multi-center case series

### Abstract

Convalescent plasma (CP) transfusion has been indicated as a promising therapy in the treatment for other emerging viral infections. However, the quality control of CP and individual variation in patients in different studies make it rather difficult to evaluate the efficacy and risk of CP therapy for coronavirus disease 2019 (COVID-19). We aimed to explore the potential efficacy of CP therapy, and to assess the possible factors associated with its efficacy. Eight critical or severe COVID-19 patients were enrolled from four centers. Each patient was transfused with 200–400 mL of CP from seven recovered donors. The primary indicators for clinical efficacy assessment were the changes of clinical symptoms, laboratory parameters, and radiological image after CP transfusion. CP donors had a wide range of antibody levels measured by serology tests which were to some degree correlated with the neutralizing antibody (NAb) level. No adverse events were observed during and after CP transfusion. Following CP

transfusion, six out of eight patients showed improved oxygen support status; chest CT indicated varying degrees of absorption of pulmonary lesions in six patients within 8 days; the viral load was decreased to a negative level in five patients who had the previous viremia; other laboratory parameters also tended to improve, including increased lymphocyte counts, decreased C-reactive protein, procalcitonin, and indicators for liver function. The clinical efficacy might be associated with CP transfusion time, transfused dose, and the NAb levels of CP. This study indicated that CP might be a potential therapy for severe patients with COVID-19.

**Reference**

https://www.nature.com/articles/s41392-020-00329-x

## A validated, real-time prediction model for favorable outcomes in hospitalized COVID-19 patients

**Abstract**

The COVID-19 pandemic has challenged front-line clinical decision-making, leading to numerous published prognostic tools. However, few models have been prospectively validated and none report implementation in practice. Here, 3345 retrospective and 474 prospective hospitalizations were used to develop and validate a parsimonious model to identify patients with favorable outcomes within 96 h of a prediction, based on real-time lab values, vital signs, and oxygen support variables. In retrospective and prospective validation, the model achieves high average precision (88.6% 95% CI: [88.4–88.7] and 90.8% [90.8–90.8]) and discrimination (95.1% [95.1–95.2] and 86.8% [86.8–86.9]) respectively. The model into the HER was implemented and integrated, achieving a positive predictive value of 93.3% with 41% sensitivity. Preliminary results suggest clinicians are adopting these scores into their clinical workflows.

**Reference**

https://www.nature.com/articles/s41746-020-00343-x

## Inference of person-to-person transmission of COVID-19 reveals hidden super-spreading events during the early outbreak phase


### Abstract

Coronavirus disease 2019 (COVID-19) was first identified in late 2019 in Wuhan, Hubei Province, China and spread globally in months, sparking worldwide concern. However, it is unclear whether super-spreading events occurred during the early outbreak phase, as has been observed for other emerging viruses. Here, 208 publicly available SARS-CoV-2 genome sequences were analysed collected during the early outbreak phase. Phylogenetic analysis was analysed with Bayesian inference under an epidemiological model to trace person-to-person transmission. The dispersion parameter of the offspring distribution in the inferred transmission chain was estimated to be 0.23 (95% CI: 0.13–0.38), indicating there are individuals who directly infected a disproportionately large number of people. Our results showed that super-spreading events played an important role in the early stage of the COVID-19 outbreak.


### Reference


https://www.nature.com/articles/s41467-020-18836-4


## The age distribution of mortality from novel coronavirus disease (COVID-19) suggests no large difference of susceptibility by age


### Abstract

Among Italy, Spain, and Japan, the age distributions of COVID-19 mortality show only small variation even though the number of deaths per country shows large variation. To understand the determinant for this situation, we constructed a mathematical model describing the transmission dynamics and natural history of COVID-19 and analyzed the dataset of mortality in Italy, Spain, and Japan. The parameter was described which describes the age-dependency of susceptibility by fitting the model to reported data, including the effect of change in contact patterns during the epidemics of COVID-19, and the fraction of symptomatic infections. Our study revealed that if the mortality rate or the fraction of symptomatic infections among all COVID-19 cases does not depend on age, then unrealistically different age-dependencies of susceptibilities against

COVID-19 infections between Italy, Japan, and Spain are required to explain the similar age distribution of mortality but different basic reproduction numbers (R0). Variation of susceptibility by age itself cannot explain the robust age distribution in mortality by COVID-19 infections in those three countries, however it does suggest that the age-dependencies of (i) the mortality rate and (ii) the fraction of symptomatic infections among all COVID-19 cases determine the age distribution of mortality by COVID-19.

**Reference**

https://www.nature.com/articles/s41598-020-73777-8

## Machine learning based early warning system enables accurate mortality risk prediction for COVID-19

**Abstract**

Soaring cases of coronavirus disease (COVID-19) are pummeling the global health system. Overwhelmed health facilities have endeavored to mitigate the pandemic, but mortality of COVID-19 continues to increase. Here, a mortality risk prediction model for COVID-19 (MRPMC) was presented that uses patients' clinical data on admission to stratify patients by mortality risk, which enables prediction of physiological deterioration and death up to 20 days in advance. This ensemble model is built using four machine learning methods including Logistic Regression, Support Vector Machine, Gradient Boosted Decision Tree, and Neural Network. MRPMC was validated in an internal validation cohort and two external validation cohorts, where it achieves an AUC of 0.9621 (95% CI: 0.9464–0.9778), 0.9760 (0.9613–0.9906), and 0.9246 (0.8763–0.9729), respectively. This model enables expeditious and accurate mortality risk stratification of patients with COVID-19, and potentially facilitates more responsive health systems that are conducive to high risk COVID-19 patients.

**Reference**

https://www.nature.com/articles/s41467-020-18684-2

## Deep phenotyping of 34,128 adult patients hospitalised with COVID-19 in an international network study


### Abstract

Comorbid conditions appear to be common among individuals hospitalised with coronavirus disease 2019 (COVID-19) but estimates of prevalence vary and little is known about the prior medication use of patients. Here, the characteristics of adults hospitalised with COVID-19 were described, and compare them with influenza patients. We include 34,128 (US: 8362, South Korea: 7341, Spain: 18,425) COVID-19 patients, summarising between 4811 and 11,643 unique aggregate characteristics. COVID-19 patients have been majority male in the US and Spain, but predominantly female in South Korea. Age profiles vary across data sources. Compared to 84,585 individuals hospitalised with influenza in 2014-19, COVID-19 patients have more typically been male, younger, and with fewer comorbidities and lower medication use. While protecting groups vulnerable to influenza is likely a useful starting point in the response to COVID-19, strategies will likely need to be broadened to reflect the particular characteristics of individuals being hospitalised with COVID-19.


### Reference


https://www.nature.com/articles/s41467-020-18849-z


**Publication Date: Oct 05, 2020**

## The utility of high-flow nasal oxygen for severe COVID-19 pneumonia in a resource-constrained setting: A multi-centre prospective observational study


### Abstract

*Background*: The utility of heated and humidified high-flow nasal oxygen (HFNO) for severe COVID-19-related hypoxaemic respiratory failure (HRF), particularly in settings with limited access to intensive care unit (ICU) resources, remains unclear, and predictors of outcome have been poorly studied.

*Methods*: Consecutive patients with COVID-19-related HRF treated with HFNO were included at two tertiary hospitals in Cape Town, South Africa. The primary outcome was

the proportion of patients who were successfully weaned from HFNO, whilst failure comprised intubation or death on HFNO.

*Findings*: The median (IQR) arterial oxygen partial pressure to fraction inspired oxygen ratio (PaO2/FiO2) was 68 (54–92) in 293 enroled patients. Of these, 137/293 (47%) of patients [PaO2/FiO2 76 (63–93)] were successfully weaned from HFNO. The median duration of HFNO was 6 (3–9) in those successfully treated versus 2 (1–5) days in those who failed (p<0.001). A higher ratio of oxygen saturation/FiO2 to respiratory rate within 6 h (ROX-6 score) after HFNO commencement was associated with HFNO success (ROX-6; AHR 0.43, 0.31–0.60), as was use of steroids (AHR 0.35, 95%CI 0.19–0.64). A ROX-6 score of ≥3.7 was 80% predictive of successful weaning whilst ROX-6 ≤ 2.2 was 74% predictive of failure. In total, 139 patents (52%) survived to hospital discharge, whilst mortality amongst HFNO failures with outcomes was 129/140 (92%).

*Interpretation*: In a resource-constrained setting, HFNO for severe COVID-19 HRF is feasible and more almost half of those who receive it can be successfully weaned without the need for mechanical ventilation.

**Reference**

https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(20)30314-X/fulltext

## Prevalence, management, and outcomes of SARS-CoV-2 infections in older people and those with dementia in mental health wards in London, UK: A retrospective observational study

**Abstract**

*Background*: People living in group situations or with dementia are more vulnerable to infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Older people and those with multimorbidity have higher mortality if they become infected than the general population. However, no systematic study exists of COVID-19-related outcomes in older inpatients in psychiatric units, who comprise people from these high-risk groups. It was aimed to describe the period prevalence, demographics, symptoms (and asymptomatic cases), management, and survival outcomes of COVID-19 in the

older inpatient psychiatric population and people with young-onset dementia in five National Health Service Trusts in London, UK, from March 1 to April 30, 2020.

*Methods*: In this retrospective observational study, we collected demographic data, mental health diagnoses, clinical diagnosis of COVID-19, symptoms, management, and COVID-19-related outcome data of inpatients aged 65 years or older or with dementia who were already inpatients or admitted as inpatients to five London mental health Trusts between March 1 and April 30, 2020, and information about available COVID-19-related resources (ie, testing and personal protective equipment). Patients were determined to have COVID-19 if they had a positive SARS-CoV-2 PCR test, or had relevant symptoms indicative of COVID-19, as determined by their treating physician. We calculated period prevalence of COVID-19 and analysed patients' characteristics, treatments, and outcomes.

*Findings*: Of 344 inpatients, 131 (38%) were diagnosed with COVID-19 during the study period (period prevalence 38% [95% CI 33–43]). The mean age of patients who had COVID-19 was 75·3 years (SD 8·2); 68 (52%) were women and 47 (36%) from ethnic minority groups. 16 (12%) of 131 patients were asymptomatic and 121 (92%) had one or more disease-related comorbidity. 108 (82%) patients were compulsorily detained. 74 (56%) patients had dementia, of whom 13 (18%) had young-onset dementia. On average, sites received COVID-19 testing kits 4·5 days after the first clinical COVID-19 presentation. 19 (15%) patients diagnosed with COVID-19 died during the study period, and their deaths were determined to be COVID-19 related.

*Interpretation*: Patients in psychiatric inpatient settings who were admitted without known SARS-CoV-2 infection had a high risk of infection with SARS-CoV-2 compared with those in the community and had a higher proportion of deaths from COVID-19 than in the community. Implementation of the long-standing policy of parity of esteem for mental health and planning for future COVID-19 waves in psychiatric hospitals is urgent.

**Reference**

https://www.thelancet.com/journals/lanpsy/article/PIIS2215-0366(20)30434-X/fulltext

## SARS-CoV-2 infection dysregulates the metabolomic and lipidomic profiles of serum


### Abstract

COVID-19 is a systemic infection that exerts significant impact on the metabolism. Yet, there is little information on how SARS-CoV-2 affects metabolism. Using NMR spectroscopy, we measured the metabolomic and lipidomic serum profile from 263 (training cohort) + 135 (validation cohort) symptomatic patients hospitalized after positive PCR testing for SARS-CoV-2 infection. We also established the profiles of 280 persons collected before the coronavirus pandemic started. PCA analyses discriminated both cohorts, highlighting the impact that the infection has in overall metabolism. The lipidomic analysis unraveled a pathogenic redistribution of the lipoprotein particle size and composition to increase the atherosclerotic risk. In turn, metabolomic analysis reveals abnormally high levels of ketone bodies (acetoacetic acid, 3-hydroxybutyric acid and acetone) and 2-hydroxybutyric acid, a readout of hepatic glutathione synthesis and marker of oxidative stress. Our results are consistent with a model in which SARS-CoV-2 infection induces liver damage associated with dyslipidemia and oxidative stress.


### Reference


https://www.cell.com/iscience/fulltext/S2589-0042(20)30837-3


## Furin, a potential therapeutic target for COVID-19


### Abstract

COVID-19 has broken out since the end of December 2019 and is still spreading rapidly, which has been listed as an international concerning public health emergency. We found the Spike protein of SARS-CoV-2 contains a furin cleavage site, which did not exist in any other betacoronavirus subtype B. Based on a series of analysis, we speculate that the presence of a redundant furin cut site in its Spike protein is responsible for SARS-CoV-2's stronger infectious than other coronaviruses, which leads to higher membrane fusion efficiency. Subsequently, a library of 4,000 compounds including approved drugs and natural products were screened against furin through structure-based virtual screening and then assayed for their inhibitory effects on furin activity. Among them, an anti-parasitic drug, Diminazene, showed the highest inhibition

effects on furin with an IC50 of 5.42 ± 0.11 μM, which might be used for the treatment of COVID-19.

**Reference**

https://www.cell.com/iscience/fulltext/S2589-0042(20)30834-8

## Health anxiety and attentional bias toward virus-related stimuli during the COVID-19 pandemic

**Abstract**

After the COVID-19 worldwide spread, evidence suggested a vast diffusion of negative consequences on people's mental health. Together with depression and sleep difficulties, anxiety symptoms seem to be the most diffused clinical outcome. The current contribution aimed to examine attentional bias for virus-related stimuli in people varying in their degree of health anxiety (HA). Consistent with previous literature, it was hypothesized that higher HA would predict attentional bias, tested using a visual dot-probe task, to virus-related stimuli. Participants were 132 Italian individuals that participated in the study during the lockdown phase in Italy. Results indicated that the HA level predicts attentional bias toward virus-related objects. This relationship is double mediated by the belief of contagion and by the consequences of contagion as assessed through a recent questionnaire developed to measure the fear for COVID-19. These findings are discussed in the context of cognitive-behavioral conceptualizations of anxiety suggesting a risk for a loop effect. Future research directions are outlined.

**Reference**

https://www.nature.com/articles/s41598-020-73599-8

## SARS-CoV-2 spike protein predicted to form complexes with host receptor protein orthologues from a broad range of mammals

**Abstract**

SARS-CoV-2 has a zoonotic origin and was transmitted to humans via an undetermined intermediate host, leading to infections in humans and other mammals. To enter host cells, the viral spike protein (S-protein) binds to its receptor, ACE2, and is then

processed by TMPRSS2. Whilst receptor binding contributes to the viral host range, S-protein:ACE2 complexes from other animals have not been investigated widely. To predict infection risks, we modelled S-protein:ACE2 complexes from 215 vertebrate species, calculated changes in the energy of the complex caused by mutations in each species, relative to human ACE2, and correlated these changes with COVID-19 infection data. We also analysed structural interactions to better understand the key residues contributing to affinity. We predict that mutations are more detrimental in ACE2 than TMPRSS2. Finally, we demonstrate phylogenetically that human SARS-CoV-2 strains have been isolated in animals. Our results suggest that SARS-CoV-2 can infect a broad range of mammals, but few fish, birds or reptiles. Susceptible animals could serve as reservoirs of the virus, necessitating careful ongoing animal management and surveillance.

**Reference**

https://www.nature.com/articles/s41598-020-71936-5

**Publication Date: Oct 03, 2020**

## A cell-based large-scale screening of natural compounds for inhibitors of SARS-CoV-2

**Abstract**

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has spread rapidly and developed into a global pandemic since its outbreak in December 2019. Currently, there is no antiviral treatment available for human use. Numerous compounds, such as remdesivir and chloroquine, have been reported to inhibit SARS-CoV-2 replication effectively *in vitro*, but for most of them, the in vivo efficacies against SARS-CoV-2 are still under clinical studies, and for chloroquine, a drug with prominent in vitro antiviral activity, it has been found no beneficial effect for COVID-19 patients in the recent largest study. It is thus urgent to speed up large-scale screening to discover drug candidates to treat COVID-19.

Recently, several high throughput screening (HTS) assays had been developed for SARS-CoV-2 antiviral discovery. A virtual screening and a fluorogenic protease

enzymatic assay based on the main protease of SARS-CoV-2 have been established to screen the protease inhibitors. A reporter gene system had been developed to screen inhibitors targeting the −1 ribosomal frameshifting of SARS-CoV-2.1 These systems select the inhibitors targeting to one specific step during infection. Here, a cytopathic effect (CPE)-based HTS assay in Vero-E6 cells was established that are permissive to SARS-CoV-2 infection to screen for inhibitors aiming to the entire viral life cyle. The antiviral efficacy of compounds was determined by the reduction of CPE, which was quantified by measuring cell viability using CCK-8 assay. The HTS conditions, including the cell density, the multiplicity of infection (MOI) and the time of incubation were first optimized in a 96-well format. The final HTS conditions were at 5000 cells/well, 0.01 of MOI, 48 h of incubation to achieve maximum assay sensitivity (producing consistently > 90% CPE in the Vero-E6 cells at endpoint) for drug screening. This assay is time-saving and allows for rapid screening of antivirals targeting the entire life cycle of SARS-CoV-2. Using this system, 1058 compounds from natural compound library were screened, and 30 hit drugs exhibiting good antiviral activities were identified, enriching the drug arsenal against SARS-CoV-2 infection.

**Reference**

https://www.nature.com/articles/s41392-020-00343-z

## Predicting the response of the dental pulp to SARS-CoV2 infection: A transcriptome-wide effect cross-analysis

**Abstract**

Pulpitis, inflammation of the dental pulp, is a disease that often necessitates emergency dental care. While pulpitis is considered to be a microbial disease primarily caused by bacteria, viruses have also been implicated in its pathogenesis. Here, we determined the expression of the SARS-CoV2 receptor, angiotensin converting enzyme 2 (ACE2) and its associated cellular serine protease TPMRSS2 in the dental pulp under normal and inflamed conditions. Next, we explored the relationship between the SARS-CoV-2/human interactome and genes expressed in pulpitis. Using existing datasets we show that both ACE2 and TPMRSS2 are expressed in the dental pulp and, that their expression does not change under conditions of inflammation. Furthermore, Master

Regulator Analysis of the SARS-CoV2/human interactome identified 75 relevant genes whose expression values are either up-regulated or down-regulated in both the human interactome and pulpitis. Our results suggest that the dental pulp is vulnerable to SARS-CoV2 infection and that SARS-CoV-2 infection of the dental pulp may contribute to worse outcomes of pulpitis.

**Reference**

https://www.nature.com/articles/s41435-020-00112-6

**Publication Date: Oct 02, 2020**

## Sarilumab use in severe SARS-CoV-2 pneumonia

**Abstract**

*Background*: Interleukin-6 signal blockade showed preliminary beneficial effects in treating inflammatory response against SARS-CoV-2 leading to severe respiratory distress. Herein we describe the outcomes of off-label intravenous use of Sarilumab in severe SARS-CoV-2-related pneumonia.

*Methods*: 53 patients with SARS-CoV-2 severe pneumonia received intravenous Sarilumab; pulmonary function improvement or Intensive Care Unit (ICU) admission rate in medical wards, live discharge rate in ICU treated patients and safety profile were recorded. Sarilumab 400 mg was administered intravenously on day 1, with eventual additional infusion based on clinical judgement, and patients were followed for at least 14 days, unless previously discharged or dead.

*Findings*: Of the 53 SARS-CoV-2pos patients receiving Sarilumab, 39(73·6%) were treated in medical wards [66·7% with a single infusion; median PaO2/FiO2:146(IQR:120–212)] while 14(26·4%) in ICU [92·6% with a second infusion; median PaO2/FiO2: 112(IQR:100–141.5)].

Within the medical wards, 7(17·9%) required ICU admission, 4 of whom were re-admitted to the ward within 5–8 days. At 19 days median follow-up, 89·7% of medical inpatients significantly improved (46·1% after 24 h, 61·5% after 3 days), 70·6% were discharged from the hospital and 85·7% no longer needed oxygen therapy. Within

patients receiving Sarilumab in ICU, 64·2% were discharged from ICU to the ward and 35·8% were still alive at the last follow-up. Overall mortality rate was 5·7%.

*Interpretation*: IL-6R inhibition appears to be a potential treatment strategy for severe SARS-CoV-2 pneumonia and intravenous Sarilumab seems a promising treatment approach showing, in the short term, an important clinical outcome and good safety.

**Reference**

https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(20)30297-2/fulltext

## Kidney function indicators predict adverse outcomes of COVID-19

**Abstract**

*Background*: The coronavirus disease 2019 (COVID-19) is an emerged respiratory infectious disease with kidney injury as a part of the clinical complications. However, the dynamic change of kidney function and its association with COVID-19 prognosis are largely unknown.

*Methods*: In this multicenter retrospective cohort study, we analyzed clinical characteristics, medical history, laboratory tests, and treatment data of 12,413 COVID-19 patients. The patient cohort was stratified according to the severity of the outcome into three groups: non-severe, severe, and death.

*Findings*: The prevalence of elevated blood urea nitrogen (BUN), elevated serum creatinine (Scr), and decreased blood uric acid (BUA) at admission was 6.29%, 5.22%, 11.66%, respectively. The trajectories showed elevation of BUN level and Scr level, as well as a reduction of BUA level during 28 days after admission in death cases. Increased all-cause mortality risk was associated with elevated baseline levels of BUN and Scr, and decreased level of BUA.

*Conclusion*: The dynamic changes of the three kidney function markers were associated with different severity and poor prognosis of COVID-19 patients. BUN showed close association and high potential for predicting adverse outcomes in COVID-19 patients for severity stratification and triage.

## Reference

https://www.cell.com/med/fulltext/S2666-6340(20)30017-9

**Benchmarking evolutionary tinkering underlying human–viral molecular mimicry shows multiple host pulmonary–arterial peptides mimicked by SARS-CoV-2**

## Abstract

The hand of molecular mimicry in shaping SARS-CoV-2 evolution and immune evasion remains to be deciphered. Here, we report 33 distinct 8-mer/9-mer peptides that are identical between SARS-CoV-2 and the human reference proteome. This observation was benchmarked against other viral–human 8-mer/9-mer peptide identity, which suggests generally similar extents of molecular mimicry for SARS-CoV-2 and many other human viruses. Interestingly, 20 novel human peptides mimicked by SARS-CoV-2 have not been observed in any previous coronavirus strains (HCoV, SARS-CoV, and MERS). Furthermore, four of the human 8-mer/9-mer peptides mimicked by SARS-CoV-2 map onto HLA-B*40:01, HLA-B*40:02, and HLA-B*35:01 binding peptides from human PAM, ANXA7, PGD, and ALOX5AP proteins. This mimicry of multiple human proteins by SARS-CoV-2 is made salient by single-cell RNA-seq (scRNA-seq) analysis that shows the targeted genes significantly expressed in human lungs and arteries; tissues implicated in COVID-19 pathogenesis. Finally, HLA-A*03 restricted 8-mer peptides are found to be shared broadly by human and coronaviridae helicases in functional hotspots, with potential implications for nucleic acid unwinding upon initial infection. This study presents the first scan of human peptide mimicry by SARS-CoV-2, and via its benchmarking against human–viral mimicry more broadly, presents a computational framework for follow-up studies to assay how evolutionary tinkering may relate to zoonosis and herd immunity.

## Reference

https://www.nature.com/articles/s41420-020-00321-y

## SARS-CoV2-mediated suppression of NRF2-signaling reveals potent antiviral and anti-inflammatory activity of 4-octyl-itaconate and dimethyl fumarate

### Abstract

Antiviral strategies to inhibit Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV2) and the pathogenic consequences of COVID-19 are urgently required. Here, we demonstrate that the NRF2 antioxidant gene expression pathway is suppressed in biopsies obtained from COVID-19 patients. Further, we uncover that NRF2 agonists 4-octyl-itaconate (4-OI) and the clinically approved dimethyl fumarate (DMF) induce a cellular antiviral program that potently inhibits replication of SARS-CoV2 across cell lines. The inhibitory effect of 4-OI and DMF extends to the replication of several other pathogenic viruses including Herpes Simplex Virus-1 and-2, Vaccinia virus, and Zika virus through a type I interferon (IFN)-independent mechanism. In addition, 4-OI and DMF limit host inflammatory responses to SARS-CoV2 infection associated with airway COVID-19 pathology. In conclusion, NRF2 agonists 4-OI and DMF induce a distinct IFN-independent antiviral program that is broadly effective in limiting virus replication and in suppressing the pro-inflammatory responses of human pathogenic viruses, including SARS-CoV2.

### Reference

https://www.nature.com/articles/s41467-020-18764-3

## Early prediction of disease progression in COVID-19 pneumonia patients with chest CT and clinical characteristics

### Abstract

The outbreak of coronavirus disease 2019 (COVID-19) has rapidly spread to become a worldwide emergency. Early identification of patients at risk of progression may facilitate more individually aligned treatment plans and optimized utilization of medical resource. Here we conducted a multicenter retrospective study involving patients with moderate COVID-19 pneumonia to investigate the utility of chest computed tomography (CT) and clinical characteristics to risk-stratify the patients. Our results show that CT severity score is associated with inflammatory levels and that older age, higher neutrophil-to-

lymphocyte ratio (NLR), and CT severity score on admission are independent risk factors for short-term progression. The nomogram based on these risk factors shows good calibration and discrimination in the derivation and validation cohorts. These findings have implications for predicting the progression risk of COVID-19 pneumonia patients at the time of admission. CT examination may help risk-stratification and guide the timing of admission.

**Reference**

https://www.nature.com/articles/s41467-020-18786-x

## The immuno-oncological challenge of COVID-19

**Abstract**

Coronavirus disease 2019 (COVID-19) and its causative virus, SARS-CoV-2, pose considerable challenges for the management of oncology patients. COVID-19 presents as a particularly severe respiratory and systemic infection in aging and immunosuppressed individuals, including patients with cancer. Moreover, severe COVID-19 is linked to an inflammatory burst and lymphopenia, which may aggravate cancer prognosis. Here we discuss why those with cancer are at higher risk of severe COVID-19, describe immune responses that confer protective or adverse reactions to this disease and indicate which antineoplastic therapies may either increase COVID-19 vulnerability or have a dual therapeutic effect on cancer and COVID-19.

**Reference**

https://www.nature.com/articles/s43018-020-00122-3

## Analysis of the clinical characteristics of 77 COVID-19 deaths

**Abstract**

COVID-19 outbreak is becoming a public health emergency. Data are limited on the clinical characteristics and causes of death. A retrospective analysis of COVID-19 deaths were performed for patients' clinical characteristics, laboratory results, and causes of death. In total, 56 patients (72.7%) of the decedents (male–female ratio 51:26, mean age 71 ± 13, mean survival time 17.4 ± 8.4 days) had comorbidities. Acute

respiratory failure (ARF) and sepsis were the main causes of death. Increases in C-reactive protein (CRP), lactate dehydrogenase (LDH), D-dimer and lactic acid and decreases in lymphocytes were common laboratory results. Intergroup analysis showed that (1) most female decedents had cough and diabetes. (2) The proportion of young- and middle-aged deaths was higher than elderly deaths for males, while elderly decedents were more prone to myocardial injury and elevated CRP. (3) CRP and LDH increased and cluster of differentiation (CD) 4+ and CD8+ cells decreased significantly in patients with hypertension. The majority of COVID-19 decedents are male, especially elderly people with comorbidities. The main causes of death are ARF and sepsis. Most female decedents have cough and diabetes. Myocardial injury is common in elderly decedents. Patients with hypertension are prone to an increased inflammatory index, tissue hypoxia and cellular immune injury.

**Reference**

https://www.nature.com/articles/s41598-020-73136-7

## Fatty monocytes in COVID-19

**Abstract**

Dysfunctional myeloid cells in patients with severe COVID-19 are linked to emergency myelopoiesis, but the exact role of these cells in the disease remains unclear. In this preprint, the authors observed that monocytes from patients with COVID-19 accumulate lipid droplets (LDs). Ex vivo exposure of healthy donor-derived monocytes to SARS-CoV-2 resulted in LD accumulation and upregulation of lipid metabolism targets. Inhibition of LD biogenesis reduced production of pro-inflammatory cytokines, viral replication and death of infected monocytes. Interestingly, the authors also showed that SARS-CoV-2 proteins and double-stranded RNA localize near LDs in infected cells. These results suggest that lipid metabolic reprogramming benefits SARS-CoV-2 infection, and its targeting in myeloid cells may have therapeutic benefit in COVID-19.

**Reference**

https://www.nature.com/articles/s41577-020-00462-2

## SARS-CoV-2 RapidPlex: A Graphene-based multiplexed telemedicine platform for rapid and low-cost COVID-19 diagnosis and monitoring

### Abstract

The COVID-19 pandemic is an ongoing global challenge for public health systems. Ultrasensitive and early identification of infection is critical to prevent widespread COVID-19 infection by presymptomatic and asymptomatic individuals, especially in the community and in-home settings. We demonstrate a multiplexed, portable, wireless electrochemical platform for ultra-rapid detection of COVID-19: the SARS-CoV-2 RapidPlex. It detects viral antigen nucleocapsid protein, IgM and IgG antibodies, as well as the inflammatory biomarker C-reactive protein, based on our mass-producible laser-engraved graphene electrodes. Ultrasensitive, highly selective, and rapid electrochemical detection in the physiologically relevant ranges was demonstrated. We successfully evaluated the applicability of our SARS-CoV-2 RapidPlex platform with COVID-19 positive and negative blood and saliva samples. Based on this pilot study, our multiplexed immunosensor platform may allow for high frequency at-home testing for COVID-19 telemedicine diagnosis and monitoring.

### Reference

https://www.cell.com/matter/fulltext/S2590-2385(20)30553-1

## Expression profiles of the SARS-CoV-2 host invasion genes in nasopharyngeal and oropharyngeal swabs of COVID-19 patients

### Abstract

The nasopharyngeal and oropharyngeal swabs of 63 subjects with severe symptoms or contacts with COVID-19 confirmed cases were collected to perform a pilot-study aimed to verify the “in situ” expression of SARS-CoV-2 host invasion genes (ACE2, TMPRSS2, PCSK3, EMILIN1, EMILIN2, MMRN1, MMRN2, DPP4). ACE2 (FC = +1.88, $p \leq 0.05$) and DPP4 (FC = +3, $p < 0.01$) genes showed a significant overexpression in COVID-19 patients. ACE2 and DPP4 expression levels had a good performance (AUC

= 0.75; p < 0.001) in distinguishing COVID-19 patients from negative subjects. Interestingly, we found a significant positive association of ACE2 mRNA and PCSK3, EMILIN1, MMRN1 and MMRN2 expression and of DPP4 mRNA and EMILIN2 expression only in COVID-19 patients. Noteworthy, a subgroup of severe COVID-19 (n = 7) patients, showed significant high level of ACE2 mRNA and another subgroup of less severe COVID-19 patients (n = 6) significant raised DPP4 levels. These results indicate that a group of SARS-CoV-2 host invasion genes are functionally related in COVID-19 patients and suggests that ACE2 and DPP4 expression level could act as genomic biomarkers. Moreover, at the best of our knowledge, this is the first study that shows an elevated DPP4 expression in naso- and oropharyngeal swabs of COVID-19 patient thus suggesting a functional role of DPP4 in SARS-CoV-2 infections.

**Reference**

https://www.cell.com/heliyon/fulltext/S2405-8440(20)31986-1

## Designing a multi-epitope peptide based vaccine against SARS-CoV-2

**Abstract**

COVID-19 pandemic has resulted in 16,114,449 cases with 646,641 deaths from the 217 countries, or territories as on July 27$^{th}$ 2020. Due to multifaceted issues and challenges in the implementation of the safety and preventive measures, inconsistent coordination between societies-governments and most importantly lack of specific vaccine to SARS-CoV-2, the spread of the virus that initially emerged at Wuhan is still uprising after taking a heavy toll on human life. In the present study, immunogenic epitopes were maped present on the four structural proteins of SARS-CoV-2 and a multi-epitope peptide based vaccine was designed that, demonstrated a high immunogenic response with a vast application on world's human population. On codon optimization and in-silico cloning, we found that candidate vaccine showed high expression in E. coli and immune simulation resulted in inducing a high level of both B-cell and T-cell mediated immunity. The results predicted that exposure of vaccine by administrating three injections significantly subsidized the antigen growth in the system. The proposed candidate vaccine found promising by yielding desired results and hence,

should be validated by practical experimentations for its functioning and efficacy to neutralize SARS-CoV-2.

**Reference**

https://www.nature.com/articles/s41598-020-73371-y

## Antiviral activity of digoxin and ouabain against SARS-CoV-2 infection and its implication for COVID-19

**Abstract**

The current coronavirus (COVID-19) pandemic is exacerbated by the absence of effective therapeutic agents. Notably, patients with COVID-19 and comorbidities such as hypertension and cardiac diseases have a higher mortality rate. An efficient strategy in response to this issue is repurposing drugs with antiviral activity for therapeutic effect. Digoxin (DIG) and ouabain (OUA) are FDA drugs for heart diseases that have antiviral activity against several coronaviruses. Thus, we aimed to assess antiviral activity of DIG and OUA against SARS-CoV-2 infection. The half-maximal inhibitory concentrations (IC50) of DIG and OUA were determined at a nanomolar concentration. Progeny virus titers of single-dose treatment of DIG, OUA and remdesivir were approximately 103-, 104- and 103-fold lower (> 99% inhibition), respectively, than that of non-treated control or chloroquine at 48 h post-infection (hpi). Furthermore, therapeutic treatment with DIG and OUA inhibited over 99% of SARS-CoV-2 replication, leading to viral inhibition at the post entry stage of the viral life cycle. Collectively, these results suggest that DIG and OUA may be an alternative treatment for COVID-19, with potential additional therapeutic effects for patients with cardiovascular disease.

**Reference**

https://www.nature.com/articles/s41598-020-72879-7

# CORRESPONDANCE

**Publication Date: Oct 03, 2020**

## Remdesivir and COVID-19

In the first published placebo-controlled trial of remdesivir for treating severe COVID-19, Yeming Wang and colleagues were unable to attain their primary endpoint of time to clinical improvement. Although admittedly underpowered due to early trial termination, remdesivir did not appear to affect rates of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) viral RNA load decline and mortality when compared with placebo. Given these disappointing findings, we are left to wonder if a lack of clinically significant outcomes in placebo-controlled trials could have been predicted. By inhibiting early coronavirus life cycle in vitro and in animal models, remdesivir might require initiation before the peak viral replication, which is not feasible in the clinical human presentation of COVID-19.

In cell cultures exposed to murine coronavirus, early remdesivir initiation substantially decreased viral titres compared with control. However, this treatment effect was completely lost when initiation occurred just 8 h after infection. In another study, mice administered early remdesivir relative to inoculation with SARS-CoV had substantially reduced lung damage compared with untreated cohorts, an effect that was lost when initiation was delayed by 2 days after inoculation. The need for early treatment has been identified in additional animal models, as Wang and colleagues confirm, with remdesivir initiation following peak viral replication being unable to affect disease severity or mortality.

**Reference**

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32021-3/fulltext

# PERSPECTIVE

**Publication Date: Oct 06, 2020**

## All surfaces are not equal in contact transmission of SARS-CoV-2

The world faces a severe and acute public health emergency due to the ongoing Coronavirus Disease 2019 (COVID-19) global pandemic caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). Healthcare workers are in the front line of the COVID-19 outbreak response and are exposed to the risk of SARS-CoV-2 infection daily. Personal protective equipment (PPE) is their main defence against viral contamination; gloves, visors, face masks and gown materials are designed to eliminate viral transfer from infected patients. Here we review research investigating the stability of SARS-CoV-2 and similar viruses on surfaces, and highlight opportunities for materials that can actively reduce SARS-CoV-2 surface contamination and associated transmission and improve PPE.

**Reference**

https://www.cell.com/matter/fulltext/S2590-2385(20)30560-9

## Cross-reactive memory T cells and herd immunity to SARS-CoV-2

Immunity is a multifaceted phenomenon. For T cell-mediated memory responses to SARS-CoV-2, it is relevant to consider their impact both on COVID-19 disease severity and on viral spread in a population. Here, we reflect on the immunological and epidemiological aspects and implications of pre-existing cross-reactive immune memory to SARS-CoV-2, which largely originates from previous exposure to circulating common cold coronaviruses. We propose four immunological scenarios for the impact of cross-reactive CD4+ memory T cells on COVID-19 severity and viral transmission. For each scenario, we discuss its implications for the dynamics of herd immunity and on projections of the global impact of SARS-CoV-2 on the human population, and assess its plausibility. In sum, we argue that key potential impacts of cross-reactive T cell memory are already incorporated into epidemiological models based on data of transmission dynamics, particularly with regard to their implications for herd immunity.

The implications of immunological processes on other aspects of SARS-CoV-2 epidemiology are worthy of future study.

**Reference**

https://www.nature.com/articles/s41577-020-00460-4

**Publication Date: Oct 05, 2020**

## The potential application of probiotics and prebiotics for the prevention and treatment of COVID-19

COVID-19 is a pandemic disease caused by the novel coronavirus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). This new viral infection was first identified in China in December 2019, and it has subsequently spread globally. The lack of a vaccine or curative treatment for COVID-19 necessitates a focus on other strategies to prevent and treat the infection. Probiotics consist of single or mixed cultures of live microorganisms that can beneficially affect the host by maintaining the intestinal or lung microbiota that play a major role in human health. At present, good scientific evidence exists to support the ability of probiotics to boost human immunity, thereby preventing colonization by pathogens and reducing the incidence and severity of infections. Herein, clinical studies were presented of the use of probiotic supplementation to prevent or treat respiratory tract infections. These data lead to promising benefits of probiotics in reducing the risk of COVID-19. Further studies should be conducted to assess the ability of probiotics to combat COVID-19.

**Reference**

https://www.nature.com/articles/s41538-020-00078-9

# COMMENT

**Publication Date: Oct 07, 2020**

## Tocilizumab is recommended for the treatment of severe COVID-19

The prospective cohort study by Mar Masiá and colleagues suggested that tocilizumab treatment of patients with severe coronavirus disease 2019 (COVID-19) does not impair the specific antibody response against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). A comparative analysis based on results from enzyme-linked immunosorbent assays, serum levels of antibodies against the SARS-CoV-2 internal nucleocapsid (N) protein (N-IgG) and surface S1 domain of the spike protein (S-IgG) was performed in 138 patients with COVID-19, and the 76 patients treated with tocilizumab showed no lower viral specific antibody response than those who had undergone other treatments. This finding suggests that use of tocilizumab to block interleukin 6 (IL-6) signaling in COVID-19 patients may be safer than expected. For more details, read the link given below.

**Reference**

https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(20)30421-7/fulltext

## Many small steps towards a COVID-19 drug

As of July 2020, more than half a million people worldwide have died of COVID-19. That number will have grown considerably by the time you read this. The research community has responded to the pandemic with unprecedented urgency. Multiple experimental vaccines have entered clinical trials—with several already in phase III—while clinicians explore potential treatments using experimental antibodies and drugs already approved for other indications. With luck, an effective vaccine will soon be available. However, it is worth remembering that while we still do not have an effective vaccine for HIV nearly three decades after its discovery, small molecule drugs have made living with the virus manageable. Creating new small molecule drugs often takes years, which is all the more reason to start early. Some promising steps towards the goal of developing a drug that specifically targets SARS-CoV-2, the coronavirus

responsible for COVID-19, are now described by Douangamath et al. in Nature Communications. Crucially, all the information reported in the manuscript was released before publication, with the idea that the wider scientific community can rapidly build upon it. For more details, read the link given below.

**Reference**

https://www.nature.com/articles/s41467-020-18710-3

**Publication Date: Oct 06, 2020**

## Do cross-reactive antibodies cause neuropathology in COVID-19?

**Abstract**

Neurological symptoms are seen in patients with COVID-19 and can persist or re-emerge after clearance of SARS-CoV-2. Recent findings suggest that antibodies to SARS-CoV-2 can cross-react with mammalian proteins. Focusing on neurological symptoms, we discuss whether these cross-reactive antibodies could contribute to COVID-19 disease pathology and to the persistence of symptoms in patients who have cleared the initial viral infection. For more details, read the link given below.

**Reference**

https://www.nature.com/articles/s41577-020-00458-y

**Publication Date: Oct 05, 2020**

## Viral arthritis and COVID-19

**Abstract**

The current outbreak of COVID-19, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is characterized by clinical signs and symptoms such as interstitial pneumonia, fatigue, and headache. Arthralgia is one of the symptoms that occurs in patients with COVID-19, and is present in 14·9% of cases. However, data on rheumatic and inflammatory manifestations (such as arthritis) are scarce.

Viral infections are a known cause of acute arthralgia and arthritis; monoarticular arthritides can occur after infection by various pathogens, including hepatitis B virus, hepatitis C virus, parvovirus, Epstein-Barr virus, HIV, alphavirus (*e. g.*, Chikungunya virus), and Zika virus. Diagnosis of viral arthritis can be difficult to confirm, nonetheless it should be considered in all patients with sudden onset of polyarticular phlogosis; to date, approximately 1% of all cases of acute inflammatory arthritis have a viral origin. For more details, read the link given below.

**Reference**

https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(20)30348-9/fulltext

## Antiviral monotherapy for hospitalised patients with COVID-19 is not enough

**Abstract**

In *The Lancet*, the RECOVERY Collaborative Group report the clinical results from the RECOVERY trial—one of the largest and most productive platform trials to date among patients admitted to hospital with COVID-19—on the effectiveness of lopinavir–ritonavir treatment. Compared with the first randomised trial to investigate lopinavir–ritonavir in patients with COVID-19 by Cao and colleagues (including the authors of this Comment), the size of the lopinavir–ritonavir group in the RECOVERY trial was much larger and hence provides a more solid evidence base regarding possible lopinavir–ritonavir treatment effects. The trial randomly allocated 5040 patients from 176 UK hospitals (3077 men and 1963 women), and the mean age of study participants was 66·2 years (SD 15·9). No differences were observed between patients assigned to lopinavir–ritonavir versus usual care in the primary outcome of 28-day all-cause mortality (rate ratio 1·03, 95% CI 0·91–1·17; p=0·60) or key secondary clinical endpoints, including duration of hospital stay and the proportion of patients discharged alive from hospital. Subgroup analyses did not find evidence for a time-to-treatment effect or benefit in those with less severe illness. The findings of these two open-label studies support each other and conclude that lopinavir–ritonavir is not effective in improving outcomes for patients admitted to hospital with COVID-19.

The authors should be commended for the large amount and high quality of work they have accomplished, but a limitation of the pragmatic design of the RECOVERY trial is

the lack of virological and biomarker data. In this regard, the previous trial in Wuhan, China, did not find evidence that lopinavir–ritonavir reduced viral RNA loads in the upper respiratory tract of patients with COVID-19. Furthermore, neither trial collected data on lopinavir exposure levels in treated patients. In any case, the results of these two trials and the similar findings with respect to a lack of mortality reduction in the WHO SOLIDARITY trial, as well as the well documented adverse effects and drug interactions caused by lopinavir–ritonavir, have led to updating of clinical management guidelines for COVID-19 to discourage use of lopinavir–ritonavir in patients admitted to hospital with COVID-19 outside of clinical trials. For more details, read the link given below.

**Reference**

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32078-X/fulltext

# HIGHLIGHTS

**Publication Date: Oct 06, 2020**

## Is smaller better? Vaccine targeting recombinant receptor-binding domain might hold the key for mass production of effective prophylactics to fight the COVID-19 pandemic


### Abstract

A recent report by Yang *et al.* published in Nature reported a recombinant vaccine utilizing recombinant receptor-binding domain (RBD) of SARS-CoV-2 Spike Protein. This vaccine candidate successfully induced potent functional antibody responses in the immunized mice, rabbits, and non-human primates. The study highlights the critical role of the immunogenicity of the RBD domain upon SARS-CoV-2 infection and the alternate vaccine designs that could serve as effective prophylactics against the pandemic.


Coronavirus disease 2019 (COVID-19) is a type of viral pneumonia that is caused by severe acute respiratory syndrome–coronavirus 2 (SARS-CoV-2). The virus is highly transmissible between humans and has spread rapidly (estimated R0 = 5.7), causing a worldwide pandemic that has had a devastating impact on global health and the world economy. As of August 8, 2020, almost 20 million people worldwide have been infected with SARS-CoV-2 and more than 750,000 deaths have been reported.2 Along with SARS-CoV and Middle East respiratory syndrome–coronavirus (MERS-CoV), SARS-CoV-2 is the third coronavirus to cause severe respiratory illness in humans. Although several drugs are under investigation to treat the disease and some have entered clinical trials, future outbreaks by related coronaviruses originating from spill-over reservoirs are highly likely. Thus, there is an urgent need to rapidly develop and deploy safe and effective vaccines to immunize an extraordinarily large number of individuals in order to protect the entire global community from the continued threat of morbidity and mortality.

Currently, the global COVID-19 vaccine R&D landscape includes more than 200 vaccine candidates, of which several have moved into clinical development. It has been structurally and functionally established that the S protein, specifically the receptor-

binding domain (RBD), binds to the angiotensin-converting enzyme 2 (ACE2) receptor on the surface of human cells to promote host cell entry, making the viral spike an attractive therapeutic and vaccine target. At least 60 vaccine platforms that are in clinical trials involve injection of one of the recombinant SARS-CoV-2 proteins to immunize a healthy individual to trigger a protective immune response against future exposures; with a large majority utilizing the spike protein. In an alternate strategy, Yang *et al.* developed a rationally designed recombinant protein vaccine comprising residues 319–545 of the SARS-CoV-2 spike-protein RBD. The recombinant protein was produced from insect cells using the Bac-to-Bac Baculovirus Expression System. Notably, proteins derived from the baculovirus expression system generally assume a correctly folded conformation and enable mass production in a relatively simple, rapid, and scalable manner making them commercially feasible. Structural insights into the purified RBD protein revealed several glycosylation sites, which were identified and mapped to ensure they may not interfere with ACE2 receptor recognition/binding.

**Reference**

https://www.nature.com/articles/s41392-020-00317-1

## SARS-CoV-2: The many pros of targeting PLpro

**Abstract**

A new study published in Nature compares the mechanisms used by SARS-CoV-1 and SARS-CoV-2 papain-like protease (PLpro) to promote innate immune evasion. Its findings identify SARS-CoV-2 PLpro as an attractive drug target for treating COVID-19.

SARS-CoV-2 is a novel human coronavirus (CoV) responsible for the COVID-19 pandemics. The pathogenesis of SARS-CoV-2 is characterized by a strong inhibition of innate immune sensing and production of type I interferon (IFN-I) responses. SARS-CoV-2 shares 79% of its genome with SARS-CoV-1, the agent responsible of the 2003 SARS epidemics, allowing comparative analyses that can address the molecular determinants in pathogenicity.

In this context, a study by Shin *et al.* aimed at identifying similarities and key differences in the activities of PLpro produced by SARS-CoV-1 (SCoV1-PLpro) and by SARS-CoV-

2 (SCoV2-PLpro). Encoded by nsp3, PLpro is one of two known CoV proteases and is required for the efficient cleavage of nsp1, nsp2, and nsp3 from the viral polyprotein, a process essential for viral genome transcription and replication. In addition to its role as a viral protease, PLpro from SARS-CoV-1 antagonizes cellular ubiquitination and ISGylation. Ubiquitination is a post-translational modification characterized by the addition of ubiquitin (Ub) chains to lysine residues of a protein, which regulates its activity, notably via its targeting to proteasomal degradation. ISGylation is a process similar to ubiquitination, where Interferon Stimulated Gene 15 (ISG15), a small protein highly induced by IFN-I, is conjugated to target proteins and modulates their functions. Both ubiquitination and ISGylation play important roles in the regulation of innate immune responses to viral infection, and it may therefore not be surprising to observe that multiple viruses have evolved different strategies to antagonize these pathways. For more details, read the link given below.

**Reference**

https://www.nature.com/articles/s41392-020-00335-z