**Long-term SARS-CoV-2 RNA shedding and its temporal association to IgG seropositivity**

**Abstract**

Longitudinal characterization of SARS-CoV-2 PCR testing from COVID-19 patient’s nasopharynx and its juxtaposition with blood-based IgG-seroconversion diagnostic assays is critical to understanding SARS-CoV-2 infection durations. Here, 851 SARS-CoV-2-positive patients were retrospectively analyzed with at least two positive PCR tests and find that 99 of these patients remain SARS-CoV-2-positive after 4 weeks from their initial diagnosis date. For the 851-patient cohort, the mean lower bound of viral RNA shedding was 17.3 days (SD: 7.8), and the mean upper bound of viral RNA shedding from 668 patients transitioning to confirmed PCR-negative status was 22.7 days (SD: 11.8). Among 104 patients with an IgG test result, 90 patients were seropositive to date, with mean upper bound of time to seropositivity from initial diagnosis being 37.8 days (95% CI: 34.3–41.3). Our findings from juxtaposing IgG and PCR tests thus reveal that some SARS-CoV-2-positive patients are non-hospitalized and seropositive, yet actively shed viral RNA (14 of 90 patients). This study emphasizes the need for monitoring viral loads and neutralizing antibody titers in long-term non-hospitalized shedders as a means of characterizing the SARS-CoV-2 infection lifecycle.

**Reference**

https://www.nature.com/articles/s41420-020-00375-y
The potential for repurposing anti-TNF as a therapy for the treatment of COVID-19

Abstract

Coronavirus disease 2019 (COVID-19) currently has few effective treatments. Given the uncertainty surrounding the effectiveness and uptake of a vaccine, it is important that the search for treatments continue. An exaggerated inflammatory state is likely responsible for much of the morbidity and mortality in COVID-19. Elevated levels of tumor necrosis factor (TNF), a key pro-inflammatory cytokine, have been shown to be associated with increased COVID-19 mortality. In patients with rheumatoid arthritis, TNF blockade reduces not only biologically active TNF but other pro-inflammatory cytokines important in COVID-19 hyperinflammation. Observational data from patients already on anti-TNF therapy show a reduced rate of COVID-19 poor outcomes and death compared with other immune-suppressing therapies. Anti-TNF has a long history of safe use, including in special at-risk populations, and is widely available. The case to adequately assess anti-TNF as a treatment for COVID-19 is compelling.

Reference

https://www.cell.com/med/fulltext/S2666-6340(20)30028-3

Sensitive, rapid, low-cost, and multiplexed COVID-19 monitoring by the wireless telemedicine platform

Abstract

To prevent the more severe spread of COVID-19 infections, sensitive, rapid, low-cost, and multiplexed detection is critical. Recently, Gao et al. reported a laser-engraved graphene-based wireless device to monitor multiple biomarkers from human biofluids, allowing for high-frequency self-testing of COVID-19 with high accuracy and low cost.

Reference

https://www.cell.com/matter/fulltext/S2590-2385(20)30618-4
Enhancement of the IFN-β-induced host signature informs repurposed drugs for COVID-19

Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a causative agent for the outbreak of coronavirus disease 2019 (COVID-19). This global pandemic is now calling for efforts to develop more effective COVID-19 therapies. Here, a host-directed approach was used, which focuses on cellular responses to diverse small-molecule treatments, to identify potentially effective drugs for COVID-19. This framework looks at the ability of compounds to elicit a similar transcriptional response to IFN-β, a type I interferon that fails to be induced at notable levels in response to SARS-CoV-2 infection. By correlating the perturbation profiles of ~3,000 small molecules with a high-quality signature of IFN-β-responsive genes in primary normal human bronchial epithelial cells, our analysis revealed four candidate COVID-19 compounds, namely homoharringtonine, narciclasine, anisomycin, and emetine. It was experimentally confirmed that the predicted compounds significantly inhibited SARS-CoV-2 replication in Vero E6 cells at nanomolar, relatively non-toxic concentrations, with half-maximal inhibitory concentrations of 165.7 nM, 16.5 nM, and 31.4 nM for homoharringtonine, narciclasine, and anisomycin, respectively. Together, our results corroborate a host-centric strategy to inform protective antiviral therapies for COVID-19.

Reference

https://www.cell.com/heliyon/fulltext/S2405-8440(20)32489-0

Publication Date: Dec 01, 2020

Fragmented health systems in COVID-19: Rectifying the misalignment between global health security and universal health coverage

Abstract

The COVID-19 pandemic has placed enormous strain on countries around the world, exposing long-standing gaps in public health and exacerbating chronic inequities. Although research and analyses have attempted to draw important lessons on how to strengthen pandemic preparedness and response, few have examined the effect that
fragmented governance for health has had on effectively mitigating the crisis. By assessing the ability of health systems to manage COVID-19 from the perspective of two key approaches to global health policy—global health security and universal health coverage—important lessons can be drawn for how to align varied priorities and objectives in strengthening health systems. This Health Policy paper compares three types of health systems (ie, with stronger investments in global health security, stronger investments in universal health coverage, and integrated investments in global health security and universal health coverage) in their response to the ongoing COVID-19 pandemic and synthesises four essential recommendations (ie, integration, financing, resilience, and equity) to reimagine governance, policies, and investments for better health towards a more sustainable future.

Reference

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32228-5/fulltext

A systematic review of corticosteroid treatment for noncritically ill patients with COVID-19

Abstract

The World Health Organization (WHO) has published guidance recommending systemic corticosteroids for the treatment of patients with severe or critical COVID-19 and no corticosteroids for those with nonsevere COVID-19. Although their recommendations for critical cases were based on the results from seven randomized controlled trials (RCTs), those for noncritical cases were based on the results from only one RCT, the Randomized Evaluation of COVID-19 Therapy (RECOVERY) trial. In search of additional evidence of corticosteroids’ effect on COVID-19, we systematically reviewed controlled observational studies, besides RCTs, that assessed the impact of corticosteroid treatment on any type of mortality and/or other outcomes in noncritical patients. Of the 4037 titles and abstracts screened, we ultimately included the RECOVERY trial and five controlled observational studies using propensity score matching, (accessed on September 8, 2020). Two of the controlled observational studies assessed the association between corticosteroid treatment and in-hospital mortality, without finding statistical significance. Four of the controlled observational studies assessed corticosteroids’ effect on other outcomes, demonstrating that they
were associated with reduced risk of intubation in patients requiring oxygen and with longer hospitalization and viral shedding in mild or moderate cases. These results support the WHO recommendations not to use corticosteroids for nonsevere COVID-19.

Reference
https://www.nature.com/articles/s41598-020-78054-2

High rate of major drug–drug interactions of lopinavir–ritonavir for COVID-19 treatment

Abstract
The impact of drug–drug interactions (DDI) between ritonavir-boosted lopinavir (LPV-r) to treat patients with coronavirus disease 2019 (COVID-19) and commonly used drugs in clinical practice is not well-known. Thus, the rate and severity of DDI between LPV-r for COVID-19 treatment and concomitant medications were evaluated. This was a cross-sectional study including all individuals diagnosed of SARS-CoV-2 infection treated with LPV-r and attended at a single center in Southern Spain (March 1st to April 30th, 2020). The frequency [95% confidence interval (95% CI)] of potential and major DDI were calculated. Overall, 469 patients were diagnosed of COVID-19, 125 (27%) of them were prescribed LPV-r. LPV-r had potential DDI with concomitant medications in 97 (78%, 95% CI 69–85%) patients, and in 33 (26%, 95% CI 19–35%) individuals showed major DDI. Twelve (36%) patients with major DDI and 14 (15%) individuals without major DDI died (p = 0.010). After adjustment, only the Charlson index was independently associated with death [adjusted OR (95% CI) for Charlson index ≥ 5: 85 (10–731), p < 0.001]. LPV-r was discontinued due to side effects in 31 (25%) patients. Management by the Infectious Diseases Unit was associated with a lower likelihood of major DDI [adjusted odds ratio (95% CI): 0.14 (0.04–0.53), p = 0.003). In conclusion, a high frequency of DDI between LPV-r for treating COVID-19 and concomitant medications was found, including major DDI. Patients with major DDI showed worse outcomes, but this association was explained by the older age and comorbidities. Patients managed by the Infectious Diseases Unit had lower risk of major DDI.

Reference
https://www.nature.com/articles/s41598-020-78029-3
Dalbavancin binds ACE2 to block its interaction with SARS-CoV-2 spike protein and is effective in inhibiting SARS-CoV-2 infection in animal models

Abstract

Infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has caused a pandemic worldwide. Currently, however, no effective drug or vaccine is available to treat or prevent the resulting coronavirus disease 2019 (COVID-19). Here, we report our discovery of a promising anti-COVID-19 drug candidate, the lipoglycopeptide antibiotic dalbavancin, based on virtual screening of the FDA-approved peptide drug library combined with in vitro and in vivo functional antiviral assays. Our results showed that dalbavancin directly binds to human angiotensin-converting enzyme 2 (ACE2) with high affinity, thereby blocking its interaction with the SARS-CoV-2 spike protein. Furthermore, dalbavancin effectively prevents SARS-CoV-2 replication in Vero E6 cells with an EC50 of ~12 nM. In both mouse and rhesus macaque models, viral replication and histopathological injuries caused by SARS-CoV-2 infection are significantly inhibited by dalbavancin administration. Given its high safety and long plasma half-life (8–10 days) shown in previous clinical trials, our data indicate that dalbavancin is a promising anti-COVID-19 drug candidate.

Reference

https://www.nature.com/articles/s41422-020-00450-0

A single-dose live-attenuated YF17D-vectored SARS-CoV-2 vaccine candidate

Abstract

The explosively expanding COVID-19 pandemic urges the development of safe, efficacious and fast-acting vaccines. Several vaccine platforms are leveraged for a rapid emergency response. The discovery of a live virus-vectored SARS-CoV-2 vaccine candidate was described using the yellow fever 17D (YF17D) vaccine as vector to express a non-cleavable prefusion form of the SARS-CoV-2 Spike antigen. Vaccine safety, immunogenicity and efficacy in several animal models were assessed. Vaccine candidate YF-S0 has an outstanding safety profile and induces high levels of SARS-CoV-2 neutralizing antibodies in hamsters, mice and cynomolgus macaques and concomitantly a protective immunity against YFV. Humoral immunity is complemented
by a favourable Th1 cell-mediated immune response as profiled in mice. In a stringent hamster model as well as in non-human primates, YF-S0 prevents infection with SARS-CoV-2. Moreover, in hamsters, a single dose confers protection from lung disease in most vaccinated animals within 10 days. Taken together, the quality of immune responses triggered and the rapid kinetics by which protective immunity can be mounted already after a single dose warrant further development this potent SARS-CoV-2 vaccine candidate.

Reference

https://www.nature.com/articles/s41586-020-3035-9

Rational development of a human antibody cocktail that deploys multiple functions to confer Pan-SARS-CoVs protection

Abstract

Structural principles underlying the composition and synergistic mechanisms of protective monoclonal antibody cocktails are poorly defined. Here, antibody cooperativity was exploited to develop a therapeutic antibody cocktail against SARS-CoV-2. On the basis of previously identified humanized cross-neutralizing antibody H014, we systematically analyzed a fully human naive antibody library and rationally identified a potent neutralizing antibody partner, P17, which confers effective protection in animal model. Cryo-EM studies dissected the nature of the P17 epitope, which is SARS-CoV-2 specific and distinctly different from that of H014. High-resolution structure of the SARS-CoV-2 spike in complex with H014 and P17, together with functional investigations revealed that in a two-antibody cocktail, synergistic neutralization was achieved by S1 shielding and conformational locking, thereby blocking receptor attachment and viral membrane fusion, conferring high potency as well as robustness against viral mutation escape. Furthermore, cluster analysis identified a hypothetical 3rd antibody partner for further reinforcing the cocktail as pan-SARS-CoVs therapeutics.

Reference

https://www.nature.com/articles/s41422-020-00444-y

Targeting the coronavirus SARS-CoV-2: Computational insights into the mechanism of action of the protease inhibitors lopinavir, ritonavir and nelfinavir
Abstract

Coronavirus SARS-CoV-2 is a recently discovered single-stranded RNA betacoronavirus, responsible for a severe respiratory disease known as coronavirus disease 2019, which is rapidly spreading. Chinese health authorities, as a response to the lack of an effective therapeutic strategy, started to investigate the use of lopinavir and ritonavir, previously optimized for the treatment and prevention of HIV/AIDS viral infection. Despite the clinical use of these two drugs, no information regarding their possible mechanism of action at the molecular level is still known for SARS-CoV-2. Very recently, the crystallographic structure of the SARS-CoV-2 main protease (Mpro), also known as C30 Endopeptidase, was published. Starting from this essential structural information, in the present work we have exploited supervised molecular dynamics, an emerging computational technique that allows investigating at an atomic level the recognition process of a ligand from its unbound to the final bound state. In this research, we provided molecular insight on the whole recognition pathway of Lopinavir, Ritonavir, and Nelfinavir, three potential C30 Endopeptidase inhibitors, with the last one taken into consideration due to the promising in-vitro activity shown against the structurally related SARS-CoV protease.

Reference

https://www.nature.com/articles/s41598-020-77700-z

**D614G spike mutation increases SARS CoV-2 susceptibility to neutralization**

Abstract

The SARS-CoV-2 Spike protein acquired a D614G mutation early in the pandemic that confers greater infectivity and is now the globally dominant form. To determine whether D614G might also mediate neutralization-escape that could compromise vaccine efficacy, sera from Spike-immunized mice, nonhuman primates and humans were evaluated for neutralization of pseudoviruses bearing either D614 or G614 spike. In all cases, the G614 pseudovirus was moderately more susceptible to neutralization. The G614 pseudovirus also was more susceptible to neutralization by receptor binding domain (RBD) monoclonal antibodies and convalescent sera from people infected with either form of the virus. Negative stain electron microscopy revealed a higher
percentage of the 1-RBD “up” conformation in the G614 spike, suggesting increased epitope exposure as a mechanism of enhanced vulnerability to neutralization. Based on these findings, the D614G mutation is not expected to be an obstacle for current vaccine development.

Reference

https://www.cell.com/cell-host-microbe/fulltext/S1931-3128(20)30634-X

**A soluble ACE2 microbody protein fused to a single immunoglobulin Fc domain is a potent inhibitor of SARS-CoV-2**

**Abstract**

Soluble forms of ACE2 have recently been shown to inhibit SARS-CoV-2 infection. It was reported on an improved soluble ACE2, termed a “microbody” in which the ACE2 ectodomain is fused to Fc domain 3 of the immunoglobulin heavy chain. The protein is smaller than previously described ACE2-Ig Fc fusion proteins and contains an H345A mutation in the ACE2 catalytic active site that inactivates the enzyme without reducing its affinity for the SARS-CoV-2 spike. The disulfide-bonded ACE2 microbody protein inhibits entry of SARS-CoV-2 spike protein pseudotyped virus and replication of live SARS-CoV-2 in vitro and in a mouse model. Its potency is 10-fold higher than soluble ACE2 and it can act after virus bound to the cell. The microbody inhibits the entry of β coronaviruses and virus with the variant D614G spike. The ACE2 microbody may be a valuable therapeutic for COVID-19 that is active against viral variants and future coronaviruses.

Reference

https://www.cell.com/cell-reports/fulltext/S2211-1247(20)31517-5

Abstract

Background: People with active cancer are recognised as at risk of COVID-19 complications, but it is unclear whether the much larger population of cancer survivors is at elevated risk. We aimed to address this by comparing cancer survivors and cancer-free controls for (i) prevalence of comorbidities considered risk factors for COVID-19; and (ii) risk of severe influenza, as a marker of susceptibility to severe outcomes from epidemic respiratory viruses.

Methods: Survivors (≥1 year) of the 20 most common cancers, and age, sex and general practice-matched cancer-free controls were included, derived from English primary care data linked to cancer registrations, hospital admissions and death registrations. Comorbidity prevalences were calculated 1 and 5 years from cancer diagnosis. Risk of hospitalisation or death due to influenza was compared using Cox models adjusted for baseline demographics and comorbidities.

Findings: 108,215 cancer survivors and 523,541 cancer-free controls were included. Cancer survivors had more diabetes, asthma, other respiratory, cardiac, neurological, renal, and liver diseases, and less obesity, compared with controls, but there was variation by cancer site. There were 205 influenza hospitalisations/deaths, with cancer survivors at higher risk than controls (adjusted HR 2.78, 95% CI 2.04–3.80). Haematological cancer survivors had large elevated risks persisting for >10 years (HR overall 15.17, 7.84–29.35; HR >10 years from cancer diagnosis 10.06, 2.47–40.93). Survivors of other cancers had evidence of raised risk up to 5 years from cancer diagnosis only (HR >5 years 2.22, 1.31–3.74).

Interpretation: Risks of severe COVID-19 outcomes are likely to be elevated in cancer survivors. This should be taken into account in policies targeted at clinical risk groups, and vaccination for both influenza, and, when available, COVID-19, should be encouraged in cancer survivors.
ELISA detection of SARS-CoV-2 antibodies in saliva

Abstract

To facilitate containment of the COVID-19 pandemic currently active in the United States and across the world, options for easy, non-invasive antibody testing are required. Here we have adapted a commercially available, serum-based enzyme-linked immunosorbent assay (ELISA) for use with saliva samples, achieving 84.2% sensitivity and 100% specificity in a set of 149 clinical samples. This strategy will enable widespread, affordable testing for patients who experienced this disease, whilst minimizing exposure risk for healthcare workers.

Reference

https://www.nature.com/articles/s41598-020-77555-4

Lethality of SARS-CoV-2 infection in K18 human angiotensin-converting enzyme 2 transgenic mice

Abstract

Vaccine and antiviral development against SARS-CoV-2 infection or COVID-19 disease would benefit from validated small animal models. Here, transgenic mice expressing human angiotensin-converting enzyme 2 (hACE2) was shown by the human cytokeratin 18 promoter (K18 hACE2) represent a susceptible rodent model. K18 hACE2 transgenic mice succumbed to SARS-CoV-2 infection by day 6, with virus detected in lung airway epithelium and brain. K18 ACE2 transgenic mice produced a modest TH1/2/17 cytokine storm in the lung and spleen that peaked by day 2, and an extended chemokine storm that was detected in both lungs and brain. This chemokine storm was also detected in the brain at day 6. K18 hACE2 transgenic mice are, therefore, highly susceptible to SARS-CoV-2 infection and represent a suitable animal model for the study of viral pathogenesis, and for identification and characterization of vaccines (prophylactic) and antivirals (therapeutics) for SARS-CoV-2 infection and associated severe COVID-19 disease.
Depletion of circulating IgM memory B cells predicts unfavourable outcome in COVID-19

Abstract

Impaired immune responses have been hypothesised to be a possible trigger of unfavourable outcomes in coronavirus disease 2019 (COVID-19). It was aimed to characterise IgM memory B cells in patients with COVID-19 admitted to an internal medicine ward in Northern Italy. Overall, 66 COVID-19 patients (mean age 74 ± 16.6 years; 29 females) were enrolled. Three patients (4.5%; 1 female) had been splenectomised and were excluded from further analyses. Fifty-five patients (87.3%) had IgM memory B cell depletion, and 18 (28.6%) died during hospitalisation (cumulative incidence rate 9.26/100 person-week; 5.8–14.7 95% CI). All patients who died had IgM memory B cell depletion. A superimposed infection was found in 6 patients (9.5%), all of them having IgM memory B cell depletion (cumulative incidence rate 3.08/100 person-week; 1.3–6.8 95% CI). At bivariable analyses, older age, sex, number of comorbidities, and peripheral blood lymphocyte count < 1500/µl were not correlated with IgM memory B cell depletion. A discrete-to-marked reduction of the B-cell compartment was also noticed in autoptic spleen specimens of two COVID-19 patients. We conclude that IgM memory B cells are commonly depleted in COVID-19 patients and this correlates with increased mortality and superimposed infections.

Reference

https://www.nature.com/articles/s41467-020-19891-7

Olfactory transmucosal SARS-CoV-2 invasion as a port of central nervous system entry in individuals with COVID-19

Abstract

The newly identified severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes COVID-19, a pandemic respiratory disease. Moreover, thromboembolic events throughout the body, including in the CNS, have been described. Given the neurological
symptoms observed in a large majority of individuals with COVID-19, SARS-CoV-2 penetrance of the CNS is likely. By various means, we demonstrate the presence of SARS-CoV-2 RNA and protein in anatomically distinct regions of the nasopharynx and brain. Furthermore, the morphological changes were described associated with infection such as thromboembolic ischemic infarction of the CNS and present evidence of SARS-CoV-2 neurotropism. SARS-CoV-2 can enter the nervous system by crossing the neural–mucosal interface in olfactory mucosa, exploiting the close vicinity of olfactory mucosal, endothelial and nervous tissue, including delicate olfactory and sensory nerve endings. Subsequently, SARS-CoV-2 appears to follow neuroanatomical structures, penetrating defined neuroanatomical areas including the primary respiratory and cardiovascular control center in the medulla oblongata.

Reference

https://www.nature.com/articles/s41593-020-00758-5

**Conserved interactions required for inhibition of the main protease of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)**

**Abstract**

The COVID-19 pandemic caused by the SARS-CoV-2 requires a fast development of antiviral drugs. SARS-CoV-2 viral main protease (Mpro, also called 3C-like protease, 3CLpro) is a potential target for drug design. Crystal and co-crystal structures of the SARS-CoV-2 Mpro have been solved, enabling the rational design of inhibitory compounds. In this study we analyzed the available SARS-CoV-2 and the highly similar SARS-CoV-1 crystal structures. We identified within the active site of the Mpro, in addition to the inhibitory ligands' interaction with the catalytic C145, two key H-bond interactions with the conserved H163 and E166 residues. Both H-bond interactions are present in almost all co-crystals and are likely to occur also during the viral polypeptide cleavage process as suggested from docking of the Mpro cleavage recognition sequence. We screened in silico a library of 6900 FDA-approved drugs (ChEMBL) and filtered using these key interactions and selected 29 non-covalent compounds predicted to bind to the protease. Additional screen, using DOCKkovalent was carried out on DrugBank library (11,414 experimental and approved drugs) and resulted in 6 covalent
compounds. The selected compounds from both screens were tested in vitro by a protease activity inhibition assay. Two compounds showed activity at the 50 µM concentration range. Our analysis and findings can facilitate and focus the development of highly potent inhibitors against SARS-CoV-2 infection.

Reference

https://www.nature.com/articles/s41598-020-77794-5

**Immunoinformatic design of a COVID-19 subunit vaccine using entire structural immunogenic epitopes of SARS-CoV-2**

**Abstract**

Coronavirus disease 2019 (COVID-19) is an acute pneumonic disease, with no prophylactic or specific therapeutical solution. Effective and rapid countermeasure against the spread of the disease’s associated virus, SARS-CoV-2, requires to incorporate the computational approach. In this study, we employed various immunoinformatics tools to design a multi-epitope vaccine polypeptide with the highest potential for activating the human immune system against SARS-CoV-2. The initial epitope set was extracted from the whole set of viral structural proteins. Potential non-toxic and non-allergenic T-cell and B-cell binding and cytokine inducing epitopes were then identified through a priori prediction. Selected epitopes were bound to each other with appropriate linkers, followed by appending a suitable adjuvant to increase the immunogenicity of the vaccine polypeptide. Molecular modelling of the 3D structure of the vaccine construct, docking, molecular dynamics simulations and free energy calculations confirmed that the vaccine peptide had high affinity for Toll-like receptor 3 binding, and that the vaccine-receptor complex was highly stable. As our vaccine polypeptide design captures the advantages of structural epitopes and simultaneously integrates precautions to avoid relevant side effects, it is suggested to be promising for elicitation of an effective and safe immune response against SARS-CoV-2 in vivo.

Reference

https://www.nature.com/articles/s41598-020-77547-4
Proteins from SARS-CoV-2 reduce T cell proliferation: A mirror image of sepsis

Abstract

Increased cytokine levels, acute phase reactants and immune checkpoint expression changes have been described in patients with Coronavirus Disease 2019 (COVID-19). Here a monocyte polarization was reported towards a low HLA-DR and high PD-L1 expression after long exposure to proteins from SARS-CoV-2. Moreover, CD86 expression was also reduced over SARS-CoV-2 proteins exposure. Additionally, T-cells proliferation was significantly reduced after stimulation with these proteins. Eventually, patients with long-term SARS-CoV-2 infection also exhibited a significant blockade of T-cells proliferation.

Reference

https://www.cell.com/heliyon/fulltext/S2405-8440(20)32478-6

Publication Date: Nov 29, 2020

COVID-19 and impairment of spermatogenesis: Implications drawn from pathological alterations in testicles and seminal parameters

Abstract

High fever may participate in impairing spermatogenesis in COVID-19 patients, given that scrotal heat stress (>39 °C) can lead to the decrease of sperm concentration and motility. However, noticeable pathological alterations in the autopsied testicular specimens of COVID-19 patients, including interstitial edema and congestion (both in testes and epididymides), red cell exudation, and obvious T-lymphocyte and macrophage infiltration around small blood vessels (both in testes and epididymides), is indicative of the other factors participate in the manifestation. IgG precipitation in seminiferous tubules is in the line of the findings observed in SARS,5 referring to orchitis of autoimmune origin. The presence of CD3+ and CD68+ cells is physiological in the epididymis, but our study reported an increased level of CD+3 and CD68+ in COVID-19 patients compared to the control. A similar finding has been reported by Xu et al. (2003) in SARS patients. For more details, read the link given below.
The effect of clinical decision making for initiation of systemic anticancer treatments in response to the COVID-19 pandemic in England: A retrospective analysis

Abstract

Background: Cancer services worldwide had to adapt in response to the COVID-19 pandemic to minimise risk to patients and staff. We aimed to assess the national impact of COVID-19 on the prescribing of systemic anticancer treatment in England, immediately after lockdown and after the introduction of new treatments to reduce patient risk.

Methods: We did a retrospective analysis using data from a central National Health Service England web database mandated for clinicians to register intention to start all new systemic anticancer treatments approved for use in England since 2016. We analysed the monthly number of treatment registrations in April, 2020, after the implementation of societal lockdown on March 23, 2020, and after implementation of treatment options to reduce patient risk such as oral or less immunosuppressive drugs, in May and June, 2020. We compared the number of registrations in April–June, 2020, with the mean number of registrations and SD during the previous 6 months of unaffected cancer care (September, 2019, to February, 2020). We calculated the percentage change and absolute difference in SD units for the number of registrations overall, by tumour type, and by type and line of therapy.

Findings: In April, 2020, 2969 registrations were recorded, representing 1417 fewer registrations than in the control period (monthly mean 4386; 32% reduction, absolute difference 4·2 SDs, p<0·0001). In May, 2020, total registrations increased to 3950, representing a 10% reduction compared with the control period (absolute difference 1·3 SDs, p<0·0001). In June, 2020, 5022 registrations were recorded, representing a 15% increase compared with the control period (absolute difference 1·9 SDs; p<0·0001).
Interpretation: After the onset of the COVID-19 pandemic, there was a reduction in systemic anticancer treatment initiation in England. However, following introduction of treatment options to reduce patient risk, registrations began to increase in May, 2020, and reached higher numbers than the pre-pandemic mean in June, 2020, when other clinical and societal risk mitigation factors (such as telephone consultations, facemasks and physical distancing) are likely to have contributed. However, outcomes of providing less treatment or delaying treatment initiation, particularly for advanced cancers and neoadjuvant therapies, require continued assessment.

Reference

https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(20)30619-7/fulltext

Dynamic changes in anti-SARS-CoV-2 antibodies during SARS-CoV-2 infection and recovery from COVID-19

Abstract

Deciphering the dynamic changes in antibodies against SARS-CoV-2 is essential for understanding the immune response in COVID-19 patients. Here we analyze the laboratory findings of 1,850 patients to describe the dynamic changes of the total antibody, spike protein (S)-, receptor-binding domain (RBD)-, and nucleoprotein (N)-specific immunoglobulin M (IgM) and G (IgG) levels during SARS-CoV-2 infection and recovery. The generation of S-, RBD-, and N-specific IgG occurs one week later in patients with severe/critical COVID-19 compared to patients with mild/moderate disease, while S- and RBD-specific IgG levels are 1.5-fold higher in severe/critical patients during hospitalization. The RBD-specific IgG levels are 4-fold higher in older patients than in younger patients during hospitalization. In addition, the S- and RBD-specific IgG levels are 2-fold higher in the recovered patients who are SARS-CoV-2 RNA negative than those who are RNA positive. Lower S-, RBD-, and N-specific IgG levels are associated with a lower lymphocyte percentage, higher neutrophil percentage, and a longer duration of viral shedding. Patients with low antibody levels on discharge might thereby have a high chance of being tested positive for SARS-CoV-2 RNA after recovery. Our study provides important information for COVID-19 diagnosis, treatment, and vaccine development.
Cellular events of acute, resolving or progressive COVID-19 in SARS-CoV-2 infected non-human primates

Abstract

Understanding SARS-CoV-2 associated immune pathology is crucial to develop pan-effective vaccines and treatments. Here we investigate the immune events from the acute state up to four weeks post SARS-CoV-2 infection, in non-human primates (NHP) with heterogeneous pulmonary pathology. We show a robust migration of CD16 expressing monocytes to the lungs occurring during the acute phase, and we describe two subsets of interstitial macrophages (HLA-DR+CD206−): A transitional CD11c+CD16+ cell population directly associated with IL-6 levels in plasma, and a long-lasting CD11b+CD16+ cell population. Trafficking of monocytes is mediated by TARC (CCL17) and associates with viral load measured in bronchial brushes. We also describe associations between disease outcomes and high levels of cell infiltration in lungs including CD11b+CD16hi macrophages and CD11b+ neutrophils. Accumulation of macrophages is long-lasting and detectable even in animals with mild or no signs of disease. Interestingly, animals with anti-inflammatory responses including high IL-10:IL-6 and kynurenine to tryptophan ratios show less severe illness. Our results unravel cellular mechanisms of COVID-19 and suggest that NHP may be appropriate models to test immune therapies.

Reference

https://www.nature.com/articles/s41467-020-19967-4

RBD-Fc-based COVID-19 vaccine candidate induces highly potent SARS-CoV-2 neutralizing antibody response

Abstract

The pandemic of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has posed serious threats to global health and economy, thus calling for the development of safe and effective vaccines.
The receptor-binding domain (RBD) in the spike protein of SARS-CoV-2 is responsible for its binding to angiotensin-converting enzyme 2 (ACE2) receptor. It contains multiple dominant neutralizing epitopes and serves as an important antigen for the development of COVID-19 vaccines. Here, it was shown that immunization of mice with a candidate subunit vaccine consisting of SARS-CoV-2 RBD and Fc fragment of human IgG, as an immunopotentiator, elicited high titer of RBD-specific antibodies with robust neutralizing activity against both pseudotyped and live SARS-CoV-2 infections. The mouse antisera could also effectively neutralize infection by pseudotyped SARS-CoV-2 with several natural mutations in RBD and the IgG extracted from the mouse antisera could also show neutralization against pseudotyped SARS-CoV and SARS-related coronavirus (SARSr-CoV). Vaccination of human ACE2 transgenic mice with RBD-Fc could effectively protect mice from the SARS-CoV-2 challenge. These results suggest that SARS-CoV-2 RBD-Fc has good potential to be further developed as an effective and broad-spectrum vaccine to prevent infection of the current SARS-CoV-2 and its mutants, as well as future emerging SARSr-CoVs and re-emerging SARS-CoV.

Reference

https://www.nature.com/articles/s41392-020-00402-5

SARS-CoV-2 genomic and subgenomic RNAs in diagnostic samples are not an indicator of active replication

Abstract

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) was first detected in late December 2019 and has spread worldwide. Coronaviruses are enveloped, positive sense, single-stranded RNA viruses and employ a complicated pattern of virus genome length RNA replication as well as transcription of genome length and leader containing subgenomic RNAs. Although not fully understood, both replication and transcription are thought to take place in so-called double-membrane vesicles in the cytoplasm of infected cells. Here we show detection of SARS-CoV-2 subgenomic RNAs in diagnostic samples up to 17 days after initial detection of infection and provide evidence for their nuclease resistance and protection by cellular membranes suggesting that detection of subgenomic RNAs in such samples may not be a suitable indicator of active coronavirus replication/infection.
Nucleocapsid protein of SARS-CoV-2 phase separates into RNA-rich polymerase-containing condensates

Abstract

The etiologic agent of the Covid-19 pandemic is the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The viral membrane of SARS-CoV-2 surrounds a helical nucleocapsid in which the viral genome is encapsulated by the nucleocapsid protein. The nucleocapsid protein of SARS-CoV-2 is produced at high levels within infected cells, enhances the efficiency of viral RNA transcription, and is essential for viral replication. Here, it was shown that RNA induces cooperative liquid–liquid phase separation of the SARS-CoV-2 nucleocapsid protein. In agreement with its ability to phase separate in vitro, we show that the protein associates in cells with stress granules, cytoplasmic RNA/protein granules that form through liquid–liquid phase separation and are modulated by viruses to maximize replication efficiency. Liquid–liquid phase separation generates high-density protein/RNA condensates that recruit the RNA-dependent RNA polymerase complex of SARS-CoV-2 providing a mechanism for efficient transcription of viral RNA. Inhibition of RNA-induced phase separation of the nucleocapsid protein by small molecules or biologics thus can interfere with a key step in the SARS-CoV-2 replication cycle.

A Multiscale coarse-grained model of the SARS-CoV-2 virion

Abstract

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the causative agent of the COVID-19 pandemic. Computer simulations of complete viral particles can provide theoretical insights into large-scale viral processes including assembly, budding, egress, entry, and fusion. Detailed atomistic simulations, however, are constrained to
shorter timescales and require billion-atom simulations for these processes. Here, the current status and on-going development of a largely “bottom-up” coarse-grained (CG) model of the SARS-CoV-2 virion were reported. Structural data from a combination of cryo-electron microscopy (cryo-EM), x-ray crystallography, and computational predictions were used to build molecular models of structural SARS-CoV-2 proteins, which were then assembled into a complete virion model. We describe how CG molecular interactions can be derived from all-atom simulations, how viral behavior difficult to capture in atomistic simulations can be incorporated into the CG models, and how the CG models can be iteratively improved as new data becomes publicly available. Our initial CG model and the detailed methods presented are intended to serve as a resource for researchers working on COVID-19 who are interested in performing multiscale simulations of the SARS-CoV-2 virion.

Reference

https://www.cell.com/biophysj/fulltext/S0006-3495(20)33168-4

**Thermal inactivation scaling applied for SARS-CoV-2**

**Abstract**

Based on a model of protein denaturation rate-limited by an entropy-related barrier, we derive a simple formula for virus inactivation time as a function of temperature. Loss of protein structure is described by two reaction coordinates: conformational disorder of the polymer and wetting by the solvent. These establish a competition between conformational entropy and hydrophobic interaction favoring random coil or globular states, respectively. Based on the Landau theory of phase transition, the resulting free energy barrier is found to decrease linearly with the temperature difference T-Tm, and the inactivation rate should scale as U to the power of T-Tm. This form recalls an accepted model of thermal damage to cells in hyperthermia. For SARS-CoV-2 the value of U in Celsius units is found to be 1.32. Although the fitting of the model to measured data is practically indistinguishable from Arrhenius law with an activation energy, the entropy barrier mechanism is more suitable and could explain the pronounced sensitivity of SARS-CoV-2 to thermal damage. Accordingly, we predict the efficacy of mild fever over a period of about 24 hours in inactivating the virus.
Remdesivir is effective in combating COVID-19 because it is a better substrate than ATP for the viral RNA-dependent RNA polymerase

Abstract

COVID-19 is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and is currently being treated using Remdesivir, a nucleoside analog that inhibits the RNA-dependent-RNA polymerase (RdRp). However, the enzymatic mechanism and efficiency of Remdesivir have not been determined, and reliable screens for new inhibitors are urgently needed. Here we present our work to optimize expression in E. coli, followed by purification and kinetic analysis of an untagged NSP12/7/8 RdRp complex. Pre-steady-state kinetic analysis shows that our reconstituted RdRp catalyzes fast (kcat = 240–680 s−1) and processive (koff = 0.013 s−1) RNA polymerization. The specificity constant (kcat/Km) for Remdesivir triphosphate (RTP) incorporation (1.29 μM−1 s−1) is higher than that for the competing ATP (0.74 μM−1 s−1). This work provides the first robust analysis of RNA polymerization and RTP incorporation by the SARS-CoV-2 RdRp and sets the standard for development of informative enzyme assays to screen for new inhibitors.

Reference

https://www.cell.com/biophysj/fulltext/S0006-3495(20)33166-0

SARS-CoV-2 spike-protein D614G mutation increases virion spike density and infectivity

Abstract

SARS-CoV-2 variants with spike (S)-protein D614G mutations now predominate globally. It was therefore compared the properties of the mutated S protein (SG614) with the original (SD614). We report here pseudoviruses carrying SG614 enter ACE2-
expressing cells more efficiently than those with SD614. This increased entry correlates with less S1-domain shedding and higher S-protein incorporation into the virion. Similar results are obtained with virus-like particles produced with SARS-CoV-2 M, N, E, and S proteins. However, D614G does not alter S-protein binding to ACE2 or neutralization sensitivity of pseudoviruses. Thus, D614G may increase infectivity by assembling more functional S protein into the virion.

Reference

https://www.nature.com/articles/s41467-020-19808-4

**HDL-scavenger receptor B type 1 facilitates SARS-CoV-2 entry**

**Abstract**

Responsible for the ongoing coronavirus disease 19 (COVID-19) pandemic, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infects host cells through binding of the viral spike protein (SARS-2-S) to the cell-surface receptor angiotensin-converting enzyme 2 (ACE2). Here we show that the high-density lipoprotein (HDL) scavenger receptor B type 1 (SR-B1) facilitates ACE2-dependent entry of SARS-CoV-2. We find that the S1 subunit of SARS-2-S binds to cholesterol and possibly to HDL components to enhance viral uptake in vitro. SR-B1 expression facilitates SARS-CoV-2 entry into ACE2-expressing cells by augmenting virus attachment. Blockade of the cholesterol-binding site on SARS-2-S1 with a monoclonal antibody, or treatment of cultured cells with pharmacological SR-B1 antagonists, inhibits HDL-enhanced SARS-CoV-2 infection. We further show that SR-B1 is coexpressed with ACE2 in human pulmonary tissue and in several extrapulmonary tissues. Our findings reveal that SR-B1 acts as a host factor that promotes SARS-CoV-2 entry and may help explain viral tropism, identify a possible molecular connection between COVID-19 and lipoprotein metabolism, and highlight SR-B1 as a potential therapeutic target to interfere with SARS-CoV-2 infection.

Reference

https://www.nature.com/articles/s42255-020-00324-0
Recurrent SARS-CoV-2 RNA positivity after COVID-19: A systematic review and meta-analysis

Abstract

Present study aimed to estimate the incidence of recurrent SARS-CoV-2 RNA positivity after recovery from COVID-19 and to determine the factors associated with recurrent positivity. We searched the PubMed, MedRxiv, BioRxiv, the Cochrane Library, ClinicalTrials.gov, and the World Health Organization International Clinical Trials Registry for studies published to June 12, 2020. Studies were reviewed to determine the risk of bias. A random-effects model was used to pool results. Heterogeneity was assessed using I². Fourteen studies of 2568 individuals were included. The incidence of recurrent SARS-CoV-2 positivity was 14.8% (95% confidence interval [CI] 11.44–18.19%). The pooled estimate of the interval from disease onset to recurrence was 35.4 days (95% CI 32.65–38.24 days), and from the last negative to the recurrent positive result was 9.8 days (95% CI 7.31–12.22 days). Patients with younger age and a longer initial illness were more likely to experience recurrent SARS-CoV-2 positivity, while patients with diabetes, severe disease, and a low lymphocyte count were less likely to experience. Present study concluded that the incidence of recurrent SARS-CoV-2 positivity was 14.8% suggesting further studies must be conducted to elucidate the possibility of infectious individuals with prolonged or recurrent RNA positivity.

Reference

https://www.nature.com/articles/s41598-020-77739-y

The central role of the nasal microenvironment in the transmission, modulation, and clinical progression of SARS-CoV-2 infection

Abstract

The novel coronavirus SARS-CoV-2 enters into the human body mainly through the ACE2 + TMPRSS2+ nasal epithelial cells. The initial host response to this pathogen occurs in a peculiar immune microenvironment that, starting from the Nasopharynx-Associated Lymphoid Tissue (NALT) system, is the product of a long evolutionary process that is aimed to first recognize exogenous airborne agents. In the present work,
we want to critically review the latest molecular and cellular findings on the mucosal response to SARS-CoV-2 in the nasal cavity and in NALT, and to analyze its impact in the subsequent course of COVID-19. Finally, we want to explore the possibility that the regulation of the systemic inflammatory network against the virus can be modulated starting from the initial phases of the nasal and nasopharyngeal response and this may have several clinical and epidemiological implications starting from a mucosal vaccine development.

Reference

https://www.nature.com/articles/s41385-020-00359-2

Genomic RNA elements drive phase separation of the sars-cov-2 nucleocapsid

Abstract

It was reported that the SARS-CoV-2 nucleocapsid protein (N-protein) undergoes liquid-liquid phase separation (LLPS) with viral RNA. N-protein condenses with specific RNA genomic elements under physiological buffer conditions and condensation is enhanced at human body temperatures (33°C and 37°C) and reduced at room temperature (22°C). RNA sequence and structure in specific genomic regions regulate N-protein condensation while other genomic regions promote condensate dissolution, potentially preventing aggregation of the large genome. At low concentrations, N-protein preferentially crosslinks to specific regions characterized by single-stranded RNA flanked by structured elements and these features specify the location, number, and strength of N-protein binding sites (valency). Liquid-like N-protein condensates form in mammalian cells in a concentration-dependent manner and can be altered by small molecules. Condensation of N-protein is RNA sequence and structure specific, sensitive to human body temperature, and manipulatable with small molecules, and therefore presents a screenable process for identifying antiviral compounds effective against SARS-CoV-2.

Reference

https://www.cell.com/molecular-cell/fulltext/S1097-2765(20)30841-8
**Nucleic acid-based technologies targeting coronaviruses**

**Abstract**

Nucleic-acid based therapies are worth developing against coronavirus (CoV) outbreaks because of their high specificity and rapid development. Several key therapeutic nucleic acid (TNA) strategies, including antisense oligonucleotides (ASOs), siRNA, and RNA-targeting clustered regularly interspaced short palindromic repeats-CRISPR-associated protein (CRISPR-Cas) technologies targeting the viral genome are potentially applicable to combat CoVs.

mRNA vaccines are attractive candidates to control CoV outbreaks with rapid/easy manufacturing, high potency, and safety. Optimal therapeutic cocktails comprising different TNAs or TNAs with other antiviral agents could act on multiple targets simultaneously, thereby enhancing antiviral effects and reducing risk of drug resistance. Lipid-ASO (LASO) nanomicelles enable cellular self-uptake and can be conjugated with antiviral molecules, providing promising anti-CoV combinational therapeutics that can be delivered directly to the lungs by aerosol. Advancement in chemical modifications and delivery vehicles remarkably enhance stability and pharmacokinetic profile of TNAs, facilitating clinical application of numerous TNAs; however, more studies on optimal chemical manufacturing and delivery methods improving safety and efficiency for TNAs are needed.

The coronavirus disease 2019 (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is currently creating a global health emergency. This crisis is driving a worldwide effort to develop effective vaccines, prophylactics, and therapeutics. Nucleic acid (NA)-based treatments hold great potential to combat outbreaks of coronaviruses (CoVs) due to their rapid development, high target specificity, and the capacity to increase druggability. Here, we review key anti-CoV NA-based technologies, including antisense oligonucleotides (ASOs), siRNAs, RNA-targeting clustered regularly interspaced short palindromic repeats-CRISPR-associated protein (CRISPR-Cas) , and mRNA vaccines, and discuss improved delivery methods and combination therapies with other antiviral drugs.
Reference

https://www.cell.com/trends/biochemical-sciences/fulltext/S0968-0004(20)30295-4

**Longitudinal multi-omics analyses identify responses of megakaryocytes, erythroid cells, and plasmablasts as hallmarks of severe COVID-19**

Abstract

Temporal resolution of cellular features associated with a severe COVID-19 disease trajectory is needed for understanding skewed immune responses and defining predictors of outcome. Here, a longitudinal multi-omics study was performed using a two-center cohort of 14 patients. We analyzed the bulk transcriptome, bulk DNA methylome, and single-cell transcriptome (>358,000 cells, including BCR profiles) of peripheral blood samples harvested from up to 5 time points. Validation was performed in two independent cohorts of COVID-19 patients. Severe COVID-19 was characterized by an increase of proliferating, metabolically hyperactive plasmablasts. Coinciding with critical illness, we also identified an expansion of interferon-activated circulating megakaryocytes and increased erythropoiesis with features of hypoxic signaling. Megakaryocyte- and erythroid-cell-derived co-expression modules were predictive of fatal disease outcome. The study demonstrates broad cellular effects of SARS-CoV-2 infection beyond adaptive immune cells and provides an entry point toward developing biomarkers and targeted treatments of patients with COVID-19.

Reference

https://www.cell.com/immunity/fulltext/S1074-7613(20)30504-5

**Low-Avidity CD4+ T cell responses to SARS-CoV-2 in unexposed individuals and humans with severe COVID-19**

CD4+ T cells reactive against SARS-CoV-2 can be found in unexposed individuals, and these are suggested to arise in response to common cold coronavirus (CCCoV) infection. Here, we utilized SARS-CoV-2-reactive CD4+ T cell enrichment to examine the antigen avidity and clonality of these cells, as well as the relative contribution of CCCoV cross-reactivity. SARS-CoV-2-reactive CD4+ memory T cells were present in virtually all unexposed individuals examined, displaying low functional avidity and
multiple, highly variable cross-reactivities that were not restricted to CCCoVs. SARS-CoV-2-reactive CD4+ T cells from COVID-19 patients lacked cross-reactivity to CCCoVs, irrespective of strong memory T cell responses against CCCoV in all donors analyzed. In severe but not mild COVID-19, SARS-CoV-2-specific T cells displayed low functional avidity and clonality, despite increased frequencies. Our findings identify low-avidity CD4+ T cell responses as a hallmark of severe COVID-19 and argue against a protective role for CCCoV-reactive T cells in SARS-CoV-2 infection.

Reference

https://www.cell.com/immunity/fulltext/S1074-7613(20)30503-3
**Risks of lung transplantation in the SARS-CoV-2 era**

As the COVID-19 pandemic has swept the world, the provision of health care for conditions that are unrelated to COVID-19 has been extensively disrupted. This is especially the case for patients in need of solid organ transplantation, and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections have complicated the approach that transplant centres must take to ensure that recipients are not placed at risk of potentially fatal outcomes or severe allograft dysfunction should they become infected with SARS-CoV-2.

Many DNA and RNA viruses pose both immediate and delayed-onset, potentially serious risks for lung transplant recipients, and disruption of host–virus relationships after solid organ transplantation can lead to both reactivation of latent viruses residing in donor tissues and new infections. Additionally, lung transplant recipients who have had successful transplantations are at risk of developing community-acquired respiratory virus infections, which have been linked to both acute and chronic lung allograft dysfunction.

**Reference**

https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30561-0/fulltext
New consensus pattern in Spike CoV-2: Potential implications in coagulation process and cell–cell fusion

Coagulopathy and syncytial formation are relevant effects of the SARS-CoV-2 infection, but the underlying molecular mechanisms triggering these processes are not fully elucidated. Here, we identified a potential consensus pattern in the Spike S glycoprotein present within the cytoplasmic domain; this consensus pattern was detected in only 79 out of 561,000 proteins (UniProt bank). Interestingly, the pattern was present in both human and bat the coronaviruses S proteins, in many proteins involved in coagulation process, cell–cell interaction, protein aggregation and regulation of cell fate, such as von Willebrand factor, coagulation factor X, fibronectin and Notch, characterized by the presence of the cysteine-rich EGF-like domain. This finding may suggest functional similarities between the matched proteins and the CoV-2 S protein, implying a new possible involvement of the S protein in the molecular mechanism that leads to the coagulopathy and cell fusion in COVID-19 disease. For more details, read the link given below.

Reference

https://www.nature.com/articles/s41420-020-00372-1
Antibiotic prescribing in general practice during COVID-19

National Health Service (NHS) England publishes monthly data on national appointment activity in general practice. The number of face-to-face appointments in this setting from April 1, to Aug 31, 2020 (46 550 551), decreased by 51·50% compared with the corresponding period in 2019 (95 975 048), whereas the number of telephone appointments increased by 270·45% (from 16 333 705 to 44 174 700) and the absolute number of appointments decreased by 20·80% (from 120 693 985 to 95 594 911). This 5 months period in 2020 comprises all data available to date following the first UK COVID-19 lockdown, which began on March 23, 2020, and progressed into the summer.

NHS England also publishes monthly data on national prescribing activity in general practice. These data include antibiotic use, which the NHS has committed to reducing to prevent antimicrobial resistance attributed to inappropriate prescribing (eg, for non-bacterial infections such as influenza or COVID-19). The number of antibiotic prescriptions made in general practice between April 1, and Aug 31, 2020, was 10 191 805, 15·48% lower than the figure for the corresponding period in 2019 (12 058 979). However, given the decrease in absolute number of appointments over this time, this number of prescriptions is 6·71% higher than expected (9 551 238)—a statistically significant increase (p<0·0001).

Reference
https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30917-8/fulltext
HIGHLIGHTS

SARS-CoV-2-induced lung pathology: AHR as a candidate therapeutic target

The aryl hydrocarbon receptor (AHR) is activated by multiple viruses to evade the host immune response, a strategy exploited in pre-clinical models to limit the replication of Zika and Influenza A. In a recent study, Liu et al. report that AHR drives the hypersecretion of lung mucins after SARS-CoV-2 infection, suggesting a role for AHR in respiratory failure and highlighting its potential therapeutic value. For more details, read the link given below.

Reference
https://www.nature.com/articles/s41422-020-00447-9
Daily briefing: UK approves Pfizer–BioNTech COVID vaccine

The United Kingdom is the first country to approve the COVID-19 vaccine developed by pharmaceutical giant Pfizer and German biotechnology company BioNTech. Hospitals, which have the ultracold freezers that are necessary to store the vaccine, had already started preparing to become the first places to roll it out next week. Conference centres and sports stadiums are being set up to support “the largest-scale vaccination campaign in our country’s history”, says Simon Stevens, the chief executive of the country’s National Health Service. Residents and staff in care homes will be the first to receive the vaccine, followed by people over 80 years old and frontline health workers. For more details, read the link given below.

Reference

https://www.nature.com/articles/d41586-020-03429-4
Predicted cellular immunity population coverage gaps for SARS-CoV-2 subunit vaccines and their augmentation by compact peptide sets

Subunit vaccines induce immunity to a pathogen by presenting a component of the pathogen and thus inherently limit the representation of pathogen peptides for cellular immunity based memory. It was found that SARS-CoV-2 subunit peptides may not be robustly displayed by the Major Histocompatibility Complex (MHC) molecules in certain individuals. An augmentation strategy was introduced for subunit vaccines that adds a small number of SARS-CoV-2 peptides to a vaccine to improve the population coverage of pathogen peptide display. Our population coverage estimates integrate clinical data on peptide immunogenicity in convalescent COVID-19 patients and machine learning predictions. The population coverage of 9 different subunits of SARS-CoV-2 was evaluated, including 5 functional domains and 4 full proteins, and augment each of them to fill a predicted coverage gap. For more details, read the link given below.

Reference

https://www.cell.com/cell-systems/fulltext/S2405-4712(20)30461-0