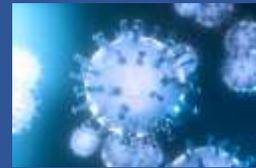


COVID-19

Jul 16-22, 2020



RESEARCH PUBLICATIONS

Publication Date: July 22, 2020

SARS-CoV-2 genomic variations associated with mortality rate of COVID-19

Abstract

The coronavirus disease 2019 (COVID-19) outbreak, caused by SARS-CoV-2, has rapidly expanded to a global pandemic. However, numbers of infected cases, deaths, and mortality rates related to COVID-19 vary from country to country. Although many studies were conducted, the reasons of these differences have not been clarified. In this study, we comprehensively investigated 12,343 SARS-CoV-2 genome sequences isolated from patients/individuals in six geographic areas and identified a total of 1234 mutations by comparing with the reference SARS-CoV-2 sequence. Through a hierarchical clustering based on the mutant frequencies, we classified the 28 countries into three clusters showing different fatality rates of COVID-19. In correlation analyses, we identified that ORF1ab 4715L and S protein 614G variants, which are in a strong linkage disequilibrium, showed significant positive correlations with fatality rates ($r = 0.41$, $P = 0.029$ and $r = 0.43$, $P = 0.022$, respectively). We found that BCG-vaccination status significantly associated with the fatality rates as well as number of infected cases. In BCG-vaccinated countries, the frequency of the S 614G variant had a trend of association with the higher fatality rate. We also found that the frequency of several HLA alleles, including HLA-A*11:01, were significantly associated with the fatality rates, although these factors were associated with number of infected cases and not an independent factor to affect fatality rate in each country. Our findings suggest that SARS-CoV-2 mutations as well as BCG-vaccination status and a host genetic factor, HLA genotypes might affect the susceptibility to SARS-CoV-2 infection or severity of COVID-19.

Reference

Retrospective Multicenter Cohort study shows early interferon therapy is associated with favorable clinical responses in COVID-19 patients

Abstract

Interferons (IFNs) are widely used in treating coronavirus disease 2019 (COVID-19) patients. However, a recent report of ACE2, the host factor mediating SARS-Cov-2 infection, identifying it as interferon-stimulated raised considerable safety concern. To examine the association between the use and timing of IFN- α 2b and clinical outcomes, we analyzed in a retrospective multicenter cohort study of 446 COVID-19 patients in Hubei, China. Regression models estimated that early administration (≤ 5 days after admission) of IFN- α 2b was associated with reduced in-hospital mortality in comparison with no admission of IFN- α 2b, whereas late administration of IFN- α 2b was associated with increased mortality. Among survivors, early IFN- α 2b was not associated with hospital discharge or computed tomography (CT) scan improvement, whereas late IFN- α 2b was associated with delayed recovery. Additionally, early IFN- α 2b and umifenovir alone or together were associated with reduced mortality and accelerated recovery in comparison with treatment with lopinavir/ritonavir (LPV/r) alone. We concluded that administration of IFN- α 2b during the early stage of COVID-19 could induce favorable clinical responses.

Reference

[https://www.cell.com/cell-host-microbe/fulltext/S1931-3128\(20\)30401-7](https://www.cell.com/cell-host-microbe/fulltext/S1931-3128(20)30401-7)

Mental health before and during the COVID-19 pandemic: A longitudinal probability sample survey of the UK population

Abstract

Background: The potential impact of the COVID-19 pandemic on population mental health is of increasing global concern. We examine changes in adult mental health in the UK population before and during the lockdown.

Methods: In this secondary analysis of a national, longitudinal cohort study, households that took part in Waves 8 or 9 of the UK Household Longitudinal Study (UKHLS) panel, including all members aged 16 or older in April, 2020, were invited to complete the COVID-19 web survey on April 23–30, 2020. Participants who were unable to make an informed decision as a result of incapacity, or who had unknown postal addresses or addresses abroad were excluded. Mental health was assessed using the 12-item General Health Questionnaire (GHQ-12). Repeated cross-sectional analyses were done to examine temporal trends. Fixed-effects regression models were fitted to identify within-person change compared with preceding trends.

Findings: Waves 6–9 of the UKHLS had 53 351 participants. Eligible participants for the COVID-19 web survey were from households that took part in Waves 8 or 9, and 17 452 (41·2%) of 42 330 eligible people participated in the web survey. Population prevalence of clinically significant levels of mental distress rose from 18·9% (95% CI 17·8–20·0) in 2018–19 to 27·3% (26·3–28·2) in April, 2020, one month into UK lockdown. Mean GHQ-12 score also increased over this time, from 11·5 (95% CI 11·3–11·6) in 2018–19, to 12·6 (12·5–12·8) in April, 2020. This was 0·48 (95% CI 0·07–0·90) points higher than expected when accounting for previous upward trends between 2014 and 2018. Comparing GHQ-12 scores within individuals, adjusting for time trends and significant predictors of change, increases were greatest in 18–24-year-olds (2·69 points, 95% CI 1·89–3·48), 25–34-year-olds (1·57, 0·96–2·18), women (0·92, 0·50–1·35), and people living with young children (1·45, 0·79–2·12). People employed before the pandemic also averaged a notable increase in GHQ-12 score (0·63, 95% CI 0·20–1·06).

Interpretation: By late April, 2020, mental health in the UK had deteriorated compared with pre-COVID-19 trends. Policies emphasising the needs of women, young people, and those with preschool aged children are likely to play an important part in preventing future mental illness.

Reference

[https://www.thelancet.com/journals/lanpsy/article/PIIS2215-0366\(20\)30308-4/fulltext](https://www.thelancet.com/journals/lanpsy/article/PIIS2215-0366(20)30308-4/fulltext)

Distinct conformational states of SARS-CoV-2 spike protein

Abstract

Intervention strategies are urgently needed to control the SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) pandemic. The trimeric viral spike (S) protein catalyzes fusion between viral and target cell membranes to initiate infection. Here we report two cryo-EM structures, derived from a preparation of the full-length S protein, representing its prefusion (2.9Å resolution) and postfusion (3.0Å resolution) conformations, respectively. The spontaneous transition to the postfusion state is independent of target cells. The prefusion trimer has three receptor-binding domains clamped down by a segment adjacent to the fusion peptide. The postfusion structure is strategically decorated by N-linked glycans, suggesting possible protective roles against host immune responses and harsh external conditions. These findings advance our understanding of SARS-CoV-2 entry and may guide development of vaccines and therapeutics.

Reference

<https://science.sciencemag.org/content/early/2020/07/20/science.abd4251>

Virus-host interactome and proteomic survey of PBMCs from COVID-19 patients reveal potential virulence factors influencing SARS-CoV-2 pathogenesis

Abstract

Background: The ongoing coronavirus disease (COVID-19) pandemic caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) is a global public health concern due to relatively easy person-to-person transmission and the current lack of

effective antiviral therapy. However, the exact molecular mechanisms of SARS-CoV-2 pathogenesis remain largely unknown.

Methods: Genome wide screening was used to establish intra-viral and viral-host interactomes. Quantitative proteomics was used to investigate peripheral blood mononuclear cell (PBMC) proteome signature in COVID-19.

Findings: We elucidated 286 host proteins targeted by SARS-CoV-2 and more than 350 host proteins that are significantly perturbed in COVID-19 derived PBMCs. This signature in severe COVID-19 PBMCs reveals significant upregulation of cellular proteins related to neutrophil activation and blood coagulation, as well as downregulation of proteins mediating T cell receptor signaling. From the interactome, we further identified that non-structural protein 10 interacts with NF-kappa-B-repressing factor (NKRF) to facilitate interleukin-8 (IL-8) induction, which potentially contributes to IL-8-mediated chemotaxis of neutrophils and the overexuberant host inflammatory response observed in COVID-19 patients.

Conclusions: Our study not only presents a systematic examination of SARS-CoV-2-induced perturbation of host targets and cellular networks but also reveals insights into the mechanisms by which SARS-CoV-2 triggers cytokine storms, representing a powerful resource in the pursuit for therapeutic intervention.

Reference

[https://www.cell.com/med/fulltext/S2666-6340\(20\)30015-5](https://www.cell.com/med/fulltext/S2666-6340(20)30015-5)

[Serial interval of SARS-CoV-2 was shortened over time by nonpharmaceutical interventions](#)

Abstract

Studies of novel coronavirus disease (COVID-19) have reported varying estimates of epidemiological parameters including serial interval distributions, i.e., the time between illness onset in successive cases in a transmission chain, and reproduction numbers. By compiling a line-list database of transmission pairs in mainland China, we show that mean serial intervals of COVID-19 have shortened substantially from 7.8 days to 2.6 days within a month (January 9 to February 13, 2020). This change is driven by enhanced non-

pharmaceutical interventions, in particular case isolation. We also show that using real-time estimation of serial intervals allowing for variation over time, provides more accurate estimates of reproduction numbers than using conventionally fixed serial interval distributions. These findings could improve assessment of transmission dynamics, forecasting future incidence, and estimating the impact of control measures.

Reference

<https://science.sciencemag.org/content/early/2020/07/20/science.abc9004>

A country level analysis measuring the impact of government actions, country preparedness and socioeconomic factors on COVID-19 mortality and related health outcomes

Abstract

Background: A country level exploratory analysis was conducted to assess the impact of timing and type of national health policy/actions undertaken towards COVID-19 mortality and related health outcomes.

Methods: Information on COVID-19 policies and health outcomes were extracted from websites and country specific sources. Data collection included the government's action, level of national preparedness, and country specific socioeconomic factors. Data was collected from the top 50 countries ranked by number of cases. Multivariable negative binomial regression was used to identify factors associated with COVID-19 mortality and related health outcomes.

Findings: Increasing COVID-19 caseloads were associated with countries with higher obesity (adjusted rate ratio [RR]=1.06; 95%CI: 1.01–1.11), median population age (RR=1.10; 95%CI: 1.05–1.15) and longer time to border closures from the first reported case (RR=1.04; 95%CI: 1.01–1.08). Increased mortality per million was significantly associated with higher obesity prevalence (RR=1.12; 95%CI: 1.06–1.19) and per capita gross domestic product (GDP) (RR=1.03; 95%CI: 1.00–1.06). Reduced income dispersion reduced mortality (RR=0.88; 95%CI: 0.83–0.93) and the number of critical cases (RR=0.92; 95% CI: 0.87–0.97). Rapid border closures, full lockdowns, and widespread testing were not associated with COVID-19 mortality per million people. However, full lockdowns (RR=2.47; 95%CI: 1.08–5.64) and reduced country vulnerability to

biological threats (i.e. high scores on the global health security scale for risk environment) (RR=1.55; 95%CI: 1.13–2.12) were significantly associated with increased patient recovery rates.

Interpretation: In this exploratory analysis, low levels of national preparedness, scale of testing and population characteristics were associated with increased national case load and overall mortality.

Reference

[https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370\(20\)30208-X/fulltext](https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(20)30208-X/fulltext)

Publication Date: July 20, 2020

Cancer increases risk of in-hospital death from COVID-19 in persons <65 years and those not in complete remission

Abstract

The impact of cancer on outcome of persons with coronavirus disease 2019 (COVID-19) after infection with acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is controversial. We studied 1859 subjects with COVID-19 from seven centers in Wuhan, China, 65 of whom had cancer. We found having cancer was an independent risk factor for in-hospital death from COVID-19 in persons <65 years (hazard ratio [HR] = 2.45, 95% confidence interval [CI], 1.04, 5.76; P = 0.041) but not in those ≥65 years (HR = 1.12 [0.56, 2.24]; P = 0.740). It was also more common in those not in complete remission. Risks of in-hospital death were similar in subjects with solid cancers and those with hematological cancers. These data may help predict outcomes of persons with cancer and COVID-19.

Reference

<https://www.nature.com/articles/s41375-020-0986-7>

Safety and immunogenicity of the ChAdOx1 nCoV-19 vaccine against SARS-CoV-2: A preliminary report of a phase 1/2, single-blind, randomised controlled trial

Abstract

Background: The pandemic of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) might be curtailed by vaccination. We assessed the safety, reactogenicity, and immunogenicity of a viral vectored coronavirus vaccine that expresses the spike protein of SARS-CoV-2.

Methods: We did a phase 1/2, single-blind, randomised controlled trial in five trial sites in the UK of a chimpanzee adenovirus-vectored vaccine (ChAdOx1 nCoV-19) expressing the SARS-CoV-2 spike protein compared with a meningococcal conjugate vaccine (MenACWY) as control. Healthy adults aged 18–55 years with no history of laboratory confirmed SARS-CoV-2 infection or of COVID-19-like symptoms were randomly assigned (1:1) to receive ChAdOx1 nCoV-19 at a dose of 5×10^{10} viral particles or MenACWY as a single intramuscular injection. A protocol amendment in two of the five sites allowed prophylactic paracetamol to be administered before vaccination. Ten participants assigned to a non-randomised, unblinded ChAdOx1 nCoV-19 prime-boost group received a two-dose schedule, with the booster vaccine administered 28 days after the first dose. Humoral responses at baseline and following vaccination were assessed using a standardised total IgG ELISA against trimeric SARS-CoV-2 spike protein, a multiplexed immunoassay, three live SARS-CoV-2 neutralisation assays (a 50% plaque reduction neutralisation assay [PRNT50]; a microneutralisation assay [MNA50, MNA80, and MNA90]; and Marburg VN), and a pseudovirus neutralisation assay. Cellular responses were assessed using an ex-vivo interferon- γ enzyme-linked immunospot assay. The co-primary outcomes are to assess efficacy, as measured by cases of symptomatic virologically confirmed COVID-19, and safety, as measured by the occurrence of serious adverse events. Analyses were done by group allocation in participants who received the vaccine. Safety was assessed over 28 days after vaccination. Here, we report the preliminary findings on safety, reactogenicity, and cellular and humoral immune responses. The study is ongoing, and was registered at ISRCTN, 15281137, and ClinicalTrials.gov, NCT04324606.

Findings: Between April 23 and May 21, 2020, 1077 participants were enrolled and assigned to receive either ChAdOx1 nCoV-19 (n=543) or MenACWY (n=534), ten of

whom were enrolled in the non-randomised ChAdOx1 nCoV-19 prime-boost group. Local and systemic reactions were more common in the ChAdOx1 nCoV-19 group and many were reduced by use of prophylactic paracetamol, including pain, feeling feverish, chills, muscle ache, headache, and malaise (all $p < 0.05$). There were no serious adverse events related to ChAdOx1 nCoV-19. In the ChAdOx1 nCoV-19 group, spike-specific T-cell responses peaked on day 14 (median 856 spot-forming cells per million peripheral blood mononuclear cells, IQR 493–1802; $n=43$). Anti-spike IgG responses rose by day 28 (median 157 ELISA units [EU], 96–317; $n=127$), and were boosted following a second dose (639 EU, 360–792; $n=10$). Neutralising antibody responses against SARS-CoV-2 were detected in 32 (91%) of 35 participants after a single dose when measured in MNA80 and in 35 (100%) participants when measured in PRNT50. After a booster dose, all participants had neutralising activity (nine of nine in MNA80 at day 42 and ten of ten in Marburg VN on day 56). Neutralising antibody responses correlated strongly with antibody levels measured by ELISA ($R^2=0.67$ by Marburg VN; $p < 0.001$).

Interpretation: ChAdOx1 nCoV-19 showed an acceptable safety profile, and homologous boosting increased antibody responses. These results, together with the induction of both humoral and cellular immune responses, support large-scale evaluation of this candidate vaccine in an ongoing phase 3 programme.

Reference

[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)31604-4/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31604-4/fulltext)

COVID-19 and cardiovascular disease: From basic mechanisms to clinical perspectives

Abstract

Coronavirus disease 2019 (COVID-19), caused by a strain of coronavirus known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has become a global pandemic that has affected the lives of billions of individuals. Extensive studies have revealed that SARS-CoV-2 shares many biological features with SARS-CoV, the zoonotic virus that caused the 2002 outbreak of severe acute respiratory syndrome, including the system of cell entry, which is triggered by binding of the viral spike protein to angiotensin-converting enzyme 2. Clinical studies have also reported an association between COVID-

19 and cardiovascular disease. Pre-existing cardiovascular disease seems to be linked with worse outcomes and increased risk of death in patients with COVID-19, whereas COVID-19 itself can also induce myocardial injury, arrhythmia, acute coronary syndrome and venous thromboembolism. Potential drug–disease interactions affecting patients with COVID-19 and comorbid cardiovascular diseases are also becoming a serious concern. In this Review, we summarize the current understanding of COVID-19 from basic mechanisms to clinical perspectives, focusing on the interaction between COVID-19 and the cardiovascular system. By combining our knowledge of the biological features of the virus with clinical findings, we can improve our understanding of the potential mechanisms underlying COVID-19, paving the way towards the development of preventative and therapeutic solutions.

Reference

<https://www.nature.com/articles/s41569-020-0413-9>

Immunogenicity and safety of a recombinant adenovirus type-5-vectored COVID-19 vaccine in healthy adults aged 18 years or older: A randomised, double-blind, placebo-controlled, phase 2 trial

Abstract

Background: This is the first randomised controlled trial for assessment of the immunogenicity and safety of a candidate non-replicating adenovirus type-5 (Ad5)-vectored COVID-19 vaccine, aiming to determine an appropriate dose of the candidate vaccine for an efficacy study.

Methods: This randomised, double-blind, placebo-controlled, phase 2 trial of the Ad5-vectored COVID-19 vaccine was done in a single centre in Wuhan, China. Healthy adults aged 18 years or older, who were HIV-negative and previous severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection-free, were eligible to participate and were randomly assigned to receive the vaccine at a dose of 1×10^{11} viral particles per mL or 5×10^{10} viral particles per mL, or placebo. Investigators allocated participants at a ratio of 2:1:1 to receive a single injection intramuscularly in the arm. The randomisation list (block size 4) was generated by an independent statistician. Participants, investigators, and staff undertaking laboratory analyses were masked to group allocation.

The primary endpoints for immunogenicity were the geometric mean titres (GMTs) of specific ELISA antibody responses to the receptor binding domain (RBD) and neutralising antibody responses at day 28. The primary endpoint for safety evaluation was the incidence of adverse reactions within 14 days. All recruited participants who received at least one dose were included in the primary and safety analyses. This study is registered with ClinicalTrials.gov, NCT04341389.

Findings: 603 volunteers were recruited and screened for eligibility between April 11 and 16, 2020. 508 eligible participants (50% male; mean age 39.7 years, SD 12.5) consented to participate in the trial and were randomly assigned to receive the vaccine (1×10^{11} viral particles $n=253$; 5×10^{10} viral particles $n=129$) or placebo ($n=126$). In the 1×10^{11} and 5×10^{10} viral particles dose groups, the RBD-specific ELISA antibodies peaked at 656.5 (95% CI 575.2–749.2) and 571.0 (467.6–697.3), with seroconversion rates at 96% (95% CI 93–98) and 97% (92–99), respectively, at day 28. Both doses of the vaccine induced significant neutralising antibody responses to live SARS-CoV-2, with GMTs of 19.5 (95% CI 16.8–22.7) and 18.3 (14.4–23.3) in participants receiving 1×10^{11} and 5×10^{10} viral particles, respectively. Specific interferon γ enzyme-linked immunospot assay responses post vaccination were observed in 227 (90%, 95% CI 85–93) of 253 and 113 (88%, 81–92) of 129 participants in the 1×10^{11} and 5×10^{10} viral particles dose groups, respectively. Solicited adverse reactions were reported by 183 (72%) of 253 and 96 (74%) of 129 participants in the 1×10^{11} and 5×10^{10} viral particles dose groups, respectively. Severe adverse reactions were reported by 24 (9%) participants in the 1×10^{11} viral particles dose group and one (1%) participant in the 5×10^{10} viral particles dose group. No serious adverse reactions were documented.

Interpretation: The Ad5-vectored COVID-19 vaccine at 5×10^{10} viral particles is safe, and induced significant immune responses in the majority of recipients after a single immunisation.

Reference

[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)31605-6/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31605-6/fulltext)

The impact of the COVID-19 pandemic on cancer deaths due to delays in diagnosis in England, UK: A national, population-based, modelling study

Abstract

Background: Since a national lockdown was introduced across the UK in March, 2020, in response to the COVID-19 pandemic, cancer screening has been suspended, routine diagnostic work deferred, and only urgent symptomatic cases prioritised for diagnostic intervention. In this study, we estimated the impact of delays in diagnosis on cancer survival outcomes in four major tumour types.

Methods: In this national population-based modelling study, we used linked English National Health Service (NHS) cancer registration and hospital administrative datasets for patients aged 15–84 years, diagnosed with breast, colorectal, and oesophageal cancer between Jan 1, 2010, and Dec 31, 2010, with follow-up data until Dec 31, 2014, and diagnosed with lung cancer between Jan 1, 2012, and Dec 31, 2012, with follow-up data until Dec 31, 2015. We use a routes-to-diagnosis framework to estimate the impact of diagnostic delays over a 12-month period from the commencement of physical distancing measures, on March 16, 2020, up to 1, 3, and 5 years after diagnosis. To model the subsequent impact of diagnostic delays on survival, we reallocated patients who were on screening and routine referral pathways to urgent and emergency pathways that are associated with more advanced stage of disease at diagnosis. We considered three reallocation scenarios representing the best to worst case scenarios and reflect actual changes in the diagnostic pathway being seen in the NHS, as of March 16, 2020, and estimated the impact on net survival at 1, 3, and 5 years after diagnosis to calculate the additional deaths that can be attributed to cancer, and the total years of life lost (YLLs) compared with pre-pandemic data.

Findings: We collected data for 32 583 patients with breast cancer, 24 975 with colorectal cancer, 6744 with oesophageal cancer, and 29 305 with lung cancer. Across the three different scenarios, compared with pre-pandemic figures, we estimate a 7.9–9.6% increase in the number of deaths due to breast cancer up to year 5 after diagnosis, corresponding to between 281 (95% CI 266–295) and 344 (329–358) additional deaths. For colorectal cancer, we estimate 1445 (1392–1591) to 1563 (1534–1592) additional deaths, a 15.3–16.6% increase; for lung cancer, 1235 (1220–1254) to 1372 (1343–1401) additional deaths, a 4.8–5.3% increase; and for oesophageal cancer, 330 (324–335) to

342 (336–348) additional deaths, 5.8–6.0% increase up to 5 years after diagnosis. For these four tumour types, these data correspond with 3291–3621 additional deaths across the scenarios within 5 years. The total additional YLLs across these cancers is estimated to be 59 204–63 229 years.

Interpretation: Substantial increases in the number of avoidable cancer deaths in England are to be expected as a result of diagnostic delays due to the COVID-19 pandemic in the UK. Urgent policy interventions are necessary, particularly the need to manage the backlog within routine diagnostic services to mitigate the expected impact of the COVID-19 pandemic on patients with cancer.

Reference

[https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045\(20\)30388-0/fulltext](https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(20)30388-0/fulltext)

Publication Date: July 19, 2020

Single-cell sequencing of peripheral blood mononuclear cells reveals distinct immune response landscapes of COVID-19 and influenza patients

Abstract

COVID-19 is a severe infectious disease that is a current global health threat. However, little is known about its hallmarks compared to other infectious diseases. Here, we report the single-cell transcriptional landscape of longitudinally collected peripheral blood mononuclear cells (PBMCs) in both COVID-19 and influenza A virus (IAV)-infected patients. We observed increase of plasma cells in both COVID-19 and IAV patients, and XAF1-, TNF- and FAS-induced T cell apoptosis in COVID-19 patients. Further analyses revealed distinct signaling pathways activated in COVID-19 (STAT1 and IRF3) vs. IAV (STAT3 and NFκB) patients and substantial differences in the expression of key factors. These factors include relatively increase of IL6R and IL6ST expression in COVID-19 patients, but similarly increased IL-6 concentrations compared to IAV patients, supporting the clinical observations of increased pro-inflammatory cytokines in COVID-19 patients. Thus, we provide the landscape of PBMCs and unveil distinct immune response pathways in COVID-19 and IAV patients.

Reference

Zhu, Linnan, Penghui Yang, Yingze Zhao, Zhenkun Zhuang, Zhifeng Wang, Rui Song, Jie Zhang et al. "Single-cell sequencing of peripheral blood mononuclear cells reveals distinct immune response landscapes of COVID-19 and influenza patients." *Immunity* (2020) (I.F.: 21.522).

Publication Date: July 17, 2020

Assessing the impact of coordinated COVID-19 exit strategies across Europe

Abstract

As rates of new COVID-19 cases decline across Europe due to non-pharmaceutical interventions such as social distancing policies and lockdown measures, countries require guidance on how to ease restrictions while minimizing the risk of resurgent outbreaks. Here, we use mobility and case data to quantify how coordinated exit strategies could delay continental resurgence and limit community transmission of COVID-19. We find that a resurgent continental epidemic could occur as many as 5 weeks earlier when well-connected countries with stringent existing interventions end their interventions prematurely. Further, we found that appropriate coordination can greatly improve the likelihood of eliminating community transmission throughout Europe. In particular, synchronizing intermittent lockdowns across Europe meant half as many lockdown periods were required to end community transmission continent-wide.

Reference

Ruktanonchai, Nick Warren, J. R. Floyd, Shengjie Lai, Corrine Warren Ruktanonchai, Adam Sadilek, Pedro Rente-Lourenco, Xue Ben et al. "Assessing the impact of coordinated COVID-19 exit strategies across Europe." *Science* (2020) (I.F. = 41.063).

Reconstruction of the full transmission dynamics of COVID-19 in Wuhan

Abstract

As countries in the world review interventions for containing the COVID-19 pandemic, important lessons can be drawn by studying the full transmission dynamics of SARS-CoV-2 in Wuhan, China, where vigorous non-pharmaceutical interventions have suppressed the local COVID-19 outbreak¹. Here, we use a modelling approach to reconstruct the full-spectrum dynamics of COVID-19 between January 1, 2020 and March 8, 2020 across five periods marked by events and interventions based on 32,583 laboratory-confirmed cases¹. Accounting for presymptomatic infectiousness², time-varying ascertainment rates, transmission rates and population movements³, we identify two key features of the outbreak: high covertness and high transmissibility. We estimate 87% (lower bound 53%) of the infections before March 8 were unascertained, potentially including asymptomatic and mild-symptomatic cases; and a basic reproduction number R_0 of 3.54 (95% credible interval [CrI]: 3.40-3.67) in the early outbreak, much higher than for SARS and MERS^{4,5}. We observe that multi-pronged interventions had considerable positive effects on controlling the outbreak, decreasing the reproduction number to 0.28 (0.23-0.33) and by projection reducing the total infections in Wuhan by 96.0% as of March 8. We furthermore explore the probability of resurgence following lifting of all interventions after 14 days of no ascertained infections, estimating it at 0.32 and 0.06 based on models with 87% and 53% unascertained infections, respectively, highlighting the risk posed by unascertained cases in changing intervention strategies. These results provide important implications for continuing surveillance and interventions to eventually contain COVID-19 outbreaks.

Reference

Hao, Xingjie, Shanshan Cheng, Degang Wu, Tangchun Wu, Xihong Lin, and Chaolong Wang. "Reconstruction of the full transmission dynamics of COVID-19 in Wuhan." *Nature* (2020): 1-7 (I.F. = 45.819).

REPORT

Publication Date: July 17, 2020

Structural basis for translational shutdown and immune evasion by the Nsp1 protein of SARS-CoV-2

SARS-CoV-2 is the causative agent of the current COVID-19 pandemic. A major virulence factor of SARS-CoVs is the nonstructural protein 1 (Nsp1) which suppresses host gene expression by ribosome association. Here, we show that Nsp1 from SARS-CoV-2 binds to the 40S ribosomal subunit, resulting in shutdown of mRNA translation both in vitro and in cells. Structural analysis by cryo-electron microscopy (cryo-EM) of in vitro reconstituted Nsp1-40S and various native Nsp1-40S and -80S complexes revealed that the Nsp1 C terminus binds to and obstructs the mRNA entry tunnel. Thereby, Nsp1 effectively blocks RIG-I-dependent innate immune responses that would otherwise facilitate clearance of the infection. Thus, the structural characterization of the inhibitory mechanism of Nsp1 may aid structure-based drug design against SARS-CoV-2.

Reference

<https://science.sciencemag.org/content/early/2020/07/16/science.abc8665>

PERSPECTIVE

Publication Date: July 17, 2020

Aging immunity may exacerbate COVID-19

Aging is associated with increased morbidity arising from a range of tissue dysfunctions. A common denominator of age-associated frailty is increased baseline inflammation, called inflammaging, that is present in older individuals. Recent studies have shown that the presence of excessive inflammation can inhibit immunity in both animals and humans and that this can be prevented by blocking inflammatory processes. This finding has important implications for the immunity of older individuals, who are infected with pathogens, such as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that induce overwhelming inflammation, which can be fatal, particularly in older people. Therefore, reducing inflammation may be a therapeutic strategy for enhancing immunity in older people, and a combination of anti-inflammatory and antiviral regimes to complement vaccination may be used as effective treatment of COVID-19 patients against the virus. For more details, see the link given below.

Reference

<https://science.sciencemag.org/content/369/6501/256>

COVID-19 revisiting inflammatory pathways of arthritis

Coronavirus disease 2019 (COVID-19) is an infectious disease, caused by severe acute respiratory syndrome coronavirus 2, which predominantly affects the lungs and, under certain circumstances, leads to an excessive or uncontrolled immune activation and cytokine response in alveolar structures. The pattern of pro-inflammatory cytokines induced in COVID-19 has similarities to those targeted in the treatment of rheumatoid arthritis. Several clinical studies are underway that test the effects of inhibiting IL-6, IL-1 β or TNF or targeting cytokine signalling via Janus kinase inhibition in the treatment of COVID-19. Despite these similarities, COVID-19 and other zoonotic coronavirus-mediated diseases do not induce clinical arthritis, suggesting that a local inflammatory niche develops in alveolar structures and drives the disease process. COVID-19 constitutes a challenge for patients with inflammatory arthritis for several reasons, in

particular, the safety of immune interventions during the pandemic. Preliminary data, however, do not suggest that patients with inflammatory arthritis are at increased risk of COVID-19. For more details, see the link given below.

Reference

Schett, Georg, Bernhard Manger, David Simon, and Roberto Caporali. "COVID-19 revisiting inflammatory pathways of arthritis." *Nature Reviews Rheumatology* (2020): 1-6 (I.F.: 18.545).

COMMENT

Publication Date: July 20, 2020

Encouraging results from phase 1/2 COVID-19 vaccine trials

Dystopian realities generate utopian visions. The dramatic emergence of SARS-CoV-2 into our lives and the subsequent COVID-19 pandemic have spawned the active development of nearly 200 vaccine candidates. Science reveals itself to the world in real time in all its glorious uncertainties, but also in all its careful, hard-won, and real achievements. As COVID-19 vaccine trials progress rapidly and with much expectation, two such achievements are published in The Lancet. The results of two early phase COVID-19 vaccine trials are reported, one from investigators at the Jenner Institute at Oxford University (Oxford, UK), with support from AstraZeneca, and the second from investigators supported by CanSino Biologics in Wuhan, China. Both groups used an adenoviral vector, and both report the vaccine achieving humoral responses to the SARS-CoV-2 spike glycoprotein receptor binding domain by day 28 as well as T-cell responses. Both report local and systemic mild adverse events such as fever, fatigue, and injection site pain. In neither trial was a severe adverse event reported. For more details, read the link given below.

Reference

[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)31611-1/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31611-1/fulltext)

NEWSLETTER

Publication Date: July 22, 2020

Coronavirus research updates: Severely ill people yield diverse trove of powerful antibodies

David Ho at Columbia University Vagelos College of Physicians and Surgeons in New York City and his colleagues (*on July 22, 2020*) have identified a diverse group of antibodies that block the new coronavirus's ability to infect cells — even when applied in low doses. The immune-system proteins called neutralizing antibodies interfere with hostile microbes trying to enter target cells. Scientists studied neutralizing antibodies from the plasma of five people with severe cases of COVID-19. Nineteen antibodies proved highly effective at preventing SARS-CoV-2 infection of cell samples.

Onya Opota and his colleagues at Lausanne University Hospital (*July 21, 2020*) analysed the viral load — the amount of virus in a standard volume of material — of samples taken from 4,172 people infected with SARS-CoV-2 between 1 February and 27 April, 2020. They noticed two distinct stages of COVID-19. Early in the disease, people have high viral loads, which tend to decline gradually as the disease progresses. This later stage is typically characterized by inflammation. The decline of viral loads could thus serve as a cue to start treating infected people with anti-inflammatory drugs.

Katie Doores at King's College London and her colleagues (*July 16, 2020*) monitored the concentration of neutralizing antibodies against SARS-CoV-2 in 65 infected people for up to 94 days. The team reports that at the peak of antibody production, people with severe COVID-19 symptoms had higher levels of antibodies than had people with mild disease. For more details, see the link given below.

Reference

<https://www.nature.com/articles/d41586-020-00502-w>

Tracking COVID-19 with artificial intelligence (July 22)

Artificial intelligence (AI) is becoming a powerful tool for tracking and treating COVID-19 in the U.S. and abroad. Several U.S. institutions are developing new AI technology or

using preexisting technology to monitor and treat the new coronavirus. HealthMap, an AI application run by Boston Children's Hospital, was launched in 2006. It was among the first tracking mechanisms to detect the COVID-19 outbreak in China. For more details, see the link given below.

Reference

<https://ge.usembassy.gov/tracking-covid-19-with-artificial-intelligence-july-22/>