COVID-19

Dec 17 - 23, 2020

RESEARCH PUBLICATIONS

Publication Date: Dec 23, 2020

Afucosylated IgG characterizes enveloped viral responses and correlates with COVID-19 severity

Abstract

IgG antibodies are crucial for protection against invading pathogens. A highly conserved N-linked glycan within the IgG-Fc tail, essential for IgG function, shows variable composition in humans. Afucosylated IgG variants are already used in anti-cancer therapeutic antibodies for their elevated activity through Fc receptors (FcγRIIIa). Here, we report that afucosylated IgG (~6% of total IgG in humans) are specifically formed against enveloped viruses but generally not against other antigens. This mediates stronger FcγRIIIa responses, but also amplifies brewing cytokine storms and immune-mediated pathologies. Critically ill COVID-19 patients, but not those with mild symptoms, had high levels of afucosylated IgG antibodies against SARS-CoV-2, amplifying pro-inflammatory cytokine release and acute phase responses. Thus, antibody glycosylation plays a critical role in immune responses to enveloped viruses, including COVID-19.

Reference

https://science.sciencemag.org/content/early/2020/12/22/science.abc8378

Safety and immunogenicity of INO-4800 DNA vaccine against SARS-CoV-2: A preliminary report of an open-label, Phase 1 clinical trial

Abstract

Background: A vaccine against SARS-CoV-2 is of high urgency. Here the safety and immunogenicity induced by a DNA vaccine (INO-4800) targeting the full length spike antigen of SARS-CoV-2 are described.

Methods: INO-4800 was evaluated in two groups of 20 participants, receiving either 1.0 mg or 2.0 mg of vaccine intradermally followed by CELLECTRA® EP at 0 and 4 weeks. Thirty-nine subjects completed both doses; one subject in the 2.0 mg group discontinued trial participation prior to receiving the second dose. ClinicalTrials.gov identifier: NCT04336410.

Findings: The median age was 34.5, 55% (22/40) were men and 82.5% (33/40) white. Through week 8, only 6 related Grade 1 adverse events in 5 subjects were observed. None of these increased in frequency with the second administration. No serious adverse events were reported. All 38 subjects evaluable for immunogenicity had cellular and/or humoral immune responses following the second dose of INO-4800. By week 6, 95% (36/38) of the participants seroconverted based on their responses by generating binding (ELISA) and/or neutralizing antibodies (PRNT IC50), with responder geometric mean binding antibody titers of 655.5 [95% CI (255.6, 1681.0)] and 994.2 [95% CI (395.3, 2500.3)] in the 1.0 mg and 2.0 mg groups, respectively. For neutralizing antibody, 78% (14/18) and 84% (16/19) generated a response with corresponding geometric mean titers of 102.3 [95% CI (37.4, 280.3)] and 63.5 [95% CI (39.6, 101.8)], in the respective groups. By week 8, 74% (14/19) and 100% (19/19) of subjects generated T cell responses by IFN-ɣ ELISpot assay with the median SFU per 106 PBMC of 46 [95% CI (21.1, 142.2)] and 71 [95% CI (32.2, 194.4)] in the 1.0 mg and 2.0 mg groups, respectively. Flow cytometry demonstrated a T cell response, dominated by CD8+ T cells co-producing IFN-ɣ and TNF-α, without increase in IL-4.

Interpretation: INO-4800 demonstrated excellent safety and tolerability and was immunogenic in 100% (38/38) of the vaccinated subjects by eliciting either or both humoral or cellular immune responses.

Reference

https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(20)30433-8/fulltext

Association of tiered restrictions and a second lockdown with COVID-19 deaths and hospital admissions in England: A modelling study

Abstract

Background: A second wave of COVID-19 cases in autumn, 2020, in England led to localised, tiered restrictions (so-called alert levels) and, subsequently, a second national lockdown. We examined the impact of these tiered restrictions, and alternatives for lockdown stringency, timing, and duration, on severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission and hospital admissions and deaths from COVID-19.

Methods: We fit an age-structured mathematical model of SARS-CoV-2 transmission to data on hospital admissions and hospital bed occupancy (ISARIC4C/COVID-19 Clinical Information Network, National Health Service [NHS] England), seroprevalence (Office for National Statistics, UK Biobank, REACT-2 study), virology (REACT-1 study), and deaths (Public Health England) across the seven NHS England regions from March 1, to Oct 13, 2020. We analysed mobility (Google Community Mobility) and social contact (CoMix study) data to estimate the effect of tiered restrictions implemented in England, and of lockdowns implemented in Northern Ireland and Wales, in October, 2020, and projected epidemiological scenarios for England up to March 31, 2021.

Findings: We estimated a reduction in the effective reproduction number (Rt) of 2% (95% credible interval [CrI] 0–4) for tier 2, 10% (6–14) for tier 3, 35% (30–41) for a Northern Ireland-stringency lockdown with schools closed, and 44% (37–49) for a Wales-stringency lockdown with schools closed. From Oct 1, 2020, to March 31, 2021, a projected COVID-19 epidemic without tiered restrictions or lockdown results in 280 000 (95% projection interval 274 000–287 000) hospital admissions and 58 500 (55 800–61 100) deaths. Tiered restrictions would reduce hospital admissions to 238 000 (231 000–245 000) and deaths to 48 600 (46 400–50 700). From Nov 5, 2020, a 4-week Wales-type lockdown with schools remaining open—similar to the lockdown measures announced in England in November, 2020—was projected to further reduce hospital

admissions to 186 000 (179 000–193 000) and deaths to 36 800 (34 900–38 800). Closing schools was projected to further reduce hospital admissions to 157 000 (152 000–163 000) and deaths to 30 300 (29 000–31 900). A projected lockdown of greater than 4 weeks would reduce deaths but would bring diminishing returns in reducing peak pressure on hospital services. An earlier lockdown would have reduced deaths and hospitalisations in the short term, but would lead to a faster resurgence in cases after January, 2021. In a post-hoc analysis, we estimated that the second lockdown in England (Nov 5–Dec 2) reduced Rt by 22% (95% CrI 15–29), rather than the 32% (25–39) reduction estimated for a Wales-stringency lockdown with schools open.

Interpretation: Lockdown measures outperform less stringent restrictions in reducing cumulative deaths. We projected that the lockdown policy announced to commence in England on Nov 5, with a similar stringency to the lockdown adopted in Wales, would reduce pressure on the health service and would be well timed to suppress deaths over the winter period, while allowing schools to remain open. Following completion of the analysis, we analysed new data from November, 2020, and found that despite similarities in policy, the second lockdown in England had a smaller impact on behaviour than did the second lockdown in Wales, resulting in more deaths and hospitalisations than we originally projected when focusing on a Wales-stringency scenario for the lockdown.

Reference

https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30984-1/fulltext

Temporal trends in severe COVID-19 outcomes in patients with rheumatic disease: A cohort study

Abstract

Background: As the COVID-19 pandemic continues worldwide, severe COVID-19 outcomes remain a major concern for patients with rheumatic and musculoskeletal diseases. We aimed to investigate temporal trends in COVID-19 outcomes in patients with rheumatic and musculoskeletal diseases over the course of the pandemic.

Methods: Using a large, multicentre, electronic health record network (TriNetX), we did a comparative cohort study of patients with rheumatic and musculoskeletal diseases who

were diagnosed with COVID-19 (by International Classification of Diseases, Tenth Revision code or positive PCR test) during the first 90 days of the pandemic (early cohort) compared with the second 90 days of the pandemic (late cohort), matched (1:1) for demographics, comorbidities, laboratory results, glucocorticoid use, and previous hospitalisations using an exposure score method. Outcomes were assessed within 30 days of COVID-19 diagnosis, including hospitalisation, intensive care unit admission, invasive mechanical ventilation, renal failure, and death. We did a subgroup analysis among patients with rheumatic and musculoskeletal diseases who were hospitalised with COVID-19.

Findings: We identified 8540 patients with rheumatic and musculoskeletal diseases who were diagnosed with COVID-19 during the 6-month study period, including 2811 in the early cohort and 5729 in the late cohort. In the exposure score matched analysis, the risk of hospitalisation was lower in the late cohort than in the early cohort (874 [32·4%] of 2701 patients *vs* 1227 [45·4%] of 2701 patients; relative risk [RR] 0·71, 95% CI 0·67–0·76). The risks of intensive care unit admission (214 [7·9%] *vs* 385 [14·3%]; RR 0·56, 95% CI 0·47–0·65), mechanical ventilation (96 [3·6%] *vs* 247 [9·1%]; 0·39, 0·31–0·49), acute kidney injury (372 [13·8%] *vs* 560 [20·7%]; 0·66, 0·59–0·75), renal replacement therapy (17 [0·6%] *vs* 32 [1·2%]; 0·53, 0·30–0·96), and death (122 [4·5%] *vs* 252 [9·3%]; 0·48, 0·39–0·60) were lower in the late cohort compared with the early cohort. Among the hospitalised subgroup, the risk of the composite outcome of intensive care unit admission, mechanical ventilation, and death was lower in the late cohort than in the early cohort (334 [30·7%] of 1089 patients *vs* 450 [41·3%] of 1089 patients; RR 0·74, 95% CI 0·67–0·83).

Interpretation: The risks of severe COVID-19 outcomes have improved over time in patients with rheumatic and musculoskeletal disease but remain substantial. These findings might reflect ascertainment of milder cases in the later cohort and improvements in treatment and supportive care.

Reference

https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(20)30422-7/fulltext

Phylogenetic supertree reveals detailed evolution of SARS-CoV-2

Abstract

Corona Virus Disease 2019 (COVID-19) caused by the emerged coronavirus SARS-CoV-2 is spreading globally. The origin of SARS-Cov-2 and its evolutionary relationship is still ambiguous. Several reports attempted to figure out this critical issue by genome-based phylogenetic analysis, yet limited progress was obtained, principally owing to the disability of these methods to reasonably integrate phylogenetic information from all genes of SARS-CoV-2. Supertree method based on multiple trees can produce the overall reasonable phylogenetic tree. However, the supertree method has been barely used for phylogenetic analysis of viruses. Here we applied the matrix representation with parsimony (MRP) pseudo-sequence supertree analysis to study the origin and evolution of SARS-CoV-2. Compared with other phylogenetic analysis methods, the supertree method showed more resolution power for phylogenetic analysis of coronaviruses. In particular, the MRP pseudo-sequence supertree analysis firmly disputes bat coronavirus RaTG13 be the last common ancestor of SARS-CoV-2, which was implied by other phylogenetic tree analysis based on viral genome sequences. Furthermore, the discovery of evolution and mutation in SARS-CoV-2 was achieved by MRP pseudo-sequence supertree analysis. Taken together, the MRP pseudo-sequence supertree provided more information on the SARS-CoV-2 evolution inference relative to the normal phylogenetic tree based on full-length genomic sequences.

Reference

https://www.nature.com/articles/s41598-020-79484-8

High affinity nanobodies block SARS-CoV-2 spike receptor binding domain interaction with human angiotensin converting enzyme

Abstract

There are currently few approved effective treatments for SARS-CoV-2, the virus responsible for the COVID-19 pandemic. Nanobodies are 12–15 kDa single-domain antibody fragments that can be delivered by inhalation and are amenable to relatively

inexpensive large scale production compared to other biologicals. We have isolated nanobodies that bind to the SARS-CoV-2 spike protein receptor binding domain and block spike protein interaction with the angiotensin converting enzyme 2 (ACE2) with 1–5 nM affinity. The lead nanobody candidate, NIH-CoVnb-112, blocks SARS-CoV-2 spike pseudotyped lentivirus infection of HEK293 cells expressing human ACE2 with an EC50 of 0.3 μg/mL. NIH-CoVnb-112 retains structural integrity and potency after nebulization. Furthermore, NIH-CoVnb-112 blocks interaction between ACE2 and several high affinity variant forms of the spike protein. These nanobodies and their derivatives have therapeutic, preventative, and diagnostic potential.

Reference

https://www.nature.com/articles/s41598-020-79036-0

Risk factors associated with 28-day all-cause mortality in older severe COVID-19 patients in Wuhan, China: A retrospective observational study

Abstract

We aimed to analyse clinical characteristics and identify risk factors predicting all-cause mortality in older patients with severe coronavirus disease 2019 (COVID-19). A total of 281 older patients with severe COVID-19 were categorized into two age groups (60–79 years and ≥ 80 years). Epidemiological, clinical, and laboratory data, and outcome were obtained. Patients aged ≥ 80 years had higher mortality (63.6%) than those aged 60–79 years (33.5%). Anorexia and comorbidities including hypertension, diabetes and COPD, higher levels of lactate dehydrogenase (LDH), osmotic pressure, C-reactive protein, D-dimer, high-sensitivity troponin I and procalcitonin, and higher SOFA scores were more common in patients aged > 80 years than those aged 60–79 years and also more common and higher in non-survivors than survivors. LDH, osmotic pressure, C-reactive protein, D-dimer, high-sensitivity troponin I, and procalcitonin were positively correlated with age and sequential organ failure assessment (SOFA), whereas CD8+ and lymphocyte counts were negatively correlated with age and SOFA. Anorexia, comorbidities including hypertension, diabetes, and chronic obstructive pulmonary disease (COPD), LDH, osmotic pressure, and SOFA were significantly associated with 28-day all-cause mortality. LDH, osmotic pressure and SOFA were valuable for predicting

28-day all-cause mortality, whereas the area under the receiver operating characteristic curve of LDH was the largest, with sensitivity of 86.0% and specificity of 80.8%. Therefore, patients with severe COVID-19 aged ≥ 80 years had worse condition and higher mortality than did those aged 60–79 years, and anorexia and comorbidities including hypertension, diabetes, COPD, elevated plasma osmotic pressure, LDH, and high SOFA were independent risk factors associated with 28-day all-cause mortality in older patients with severe COVID-19. LDH may have the highest predictive value for 28-day all-cause mortality in all examined factors.

Reference

https://www.nature.com/articles/s41598-020-79508-3

Calcium channel blocker amlodipine besylate therapy is associated with reduced case fatality rate of COVID-19 patients with hypertension

Abstract

The coronavirus disease (COVID-19) caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has now spread to >200 countries posing a global public health concern. Patients with comorbidity, such as hypertension suffer more severe infection with elevated mortality. The development of effective antiviral drugs is in urgent need to treat COVID-19 patients. Here, we report that calcium channel blockers (CCBs), a type of antihypertensive drug that is widely used in clinics, inhibited the post-entry replication events of SARS-CoV-2 in vitro, while no in vitro anti-SARS-CoV-2 effect was observed for the two other major types of antihypertensive drugs, namely, angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers. CCB combined with chloroquine showed a significantly enhanced anti-SARS-CoV-2 efficacy. A retrospective clinical investigation on hospitalized COVID-19 patients with hypertension as the only comorbidity revealed that the CCB amlodipine besylate therapy was associated with a decreased case fatality rate. The results from this study suggest that CCB administration to COVID-19 patients with hypertension as the comorbidity might improve the disease outcome.

Reference

https://www.nature.com/articles/s41421-020-00235-0

Compromised SARS-CoV-2-specific placental antibody transfer

Abstract

SARS-CoV-2 infection causes more severe disease in pregnant women compared to age-matched non-pregnant women. Whether maternal infection causes changes in the transfer of immunity to infants remains unclear. Maternal infections have previously been associated with compromised placental antibody transfer, but the mechanism underlying this compromised transfer is not established. Here, we used systems serology to characterize the Fc-profile of influenza-, pertussis-, and SARS-CoV-2-specific antibodies transferred across the placenta. Influenza- and pertussis-specific antibodies were actively transferred. However, SARS-CoV-2-specific antibody transfer was significantly reduced compared to influenza- and pertussis-specific antibodies, and cord titers and functional activity were lower than in maternal plasma. This effect was only observed in third trimester infection. SARS-CoV-2-specific transfer was linked to altered SARS-CoV-2-antibody glycosylation profiles and was partially rescued by infection-induced increases in IgG and increased FCGR3A placental expression. These results point to unexpected compensatory mechanisms to boost immunity in neonates, providing insights for maternal vaccine design.

Reference

https://www.cell.com/cell/fulltext/S0092-8674(20)31749-9

The persistence of interleukin-6 is regulated by a blood buffer system derived from dendritic cells

Abstract

The interleukin-6 (IL-6) membrane receptor and its circulating soluble form, sIL-6R, can be targeted by antibody therapy to reduce deleterious immune signaling caused by chronic overexpression of the pro-inflammatory cytokine IL-6. This strategy may also hold promise for treating acute hyperinflammation, such as observed in coronavirus disease

2019 (COVID-19), highlighting a need to define regulators of IL-6 homeostasis. We found that conventional dendritic cells (cDCs), defined in mice via expression of the transcription factor Zbtb46, were a major source of circulating sIL-6R and, thus, systemically regulated IL-6 signaling. This was uncovered through identification of a cDC-dependent but T cell-independent modality that naturally adjuvants plasma cell differentiation and antibody responses to protein antigens. This pathway was then revealed as part of a broader biological buffer system in which cDC-derived sIL-6R set the in-solution persistence of IL-6. This control axis may further inform the development of therapeutic agents to modulate pro-inflammatory immune reactions.

Reference

https://www.cell.com/immunity/fulltext/S1074-7613(20)30508-2

Neurological manifestations of COVID-19 feature T-Cell exhaustion and dedifferentiated monocytes in cerebrospinal fluid

Abstract

Patients suffering from Coronavirus disease 2019 (COVID-19) can develop neurological sequelae, such as headache, neuroinflammatory or cerebrovascular disease. These conditions - here termed Neuro-COVID - are more frequent in patients with severe COVID-19. To understand the etiology of these neurological sequelae, we utilized single-cell sequencing and examined the immune cell profiles from the cerebrospinal fluid (CSF) of Neuro-COVID patients compared to patients with non-inflammatory and autoimmune neurological diseases or with viral encephalitis. The CSF of Neuro-COVID patients exhibited an expansion of dedifferentiated monocytes and of exhausted CD4+ T cells. Neuro-COVID CSF leukocytes featured an enriched interferon signature; however, this was less pronounced than in viral encephalitis. Repertoire analysis revealed broad clonal T cell expansion and curtailed interferon response in severe compared to mild Neuro-COVID patients. Collectively, our findings document the CSF immune compartment in Neuro-COVID patients and suggest compromised antiviral responses in this setting.

Reference

https://www.cell.com/immunity/fulltext/S1074-7613(20)30539-2

The SARS-CoV-2 RNA–protein interactome in infected human cells

Abstract

Characterizing the interactions that SARS-CoV-2 viral RNAs make with host cell proteins during infection can improve our understanding of viral RNA functions and the host innate immune response. Using RNA antisense purification and mass spectrometry, we identified up to 104 human proteins that directly and specifically bind to SARS-CoV-2 RNAs in infected human cells. We integrated the SARS-CoV-2 RNA interactome with changes in proteome abundance induced by viral infection and linked interactome proteins to cellular pathways relevant to SARS-CoV-2 infections. We demonstrated by genetic perturbation that cellular nucleic acid-binding protein (CNBP) and La-related protein 1 (LARP1), two of the most strongly enriched viral RNA binders, restrict SARS-CoV-2 replication in infected cells and provide a global map of their direct RNA contact sites. Pharmacological inhibition of three other RNA interactome members, PPIA, ATP1A1, and the ARP2/3 complex, reduced viral replication in two human cell lines. The identification of host dependency factors and defence strategies as presented in this work will improve the design of targeted therapeutics against SARS-CoV-2.

Reference

https://www.nature.com/articles/s41564-020-00846-z

Underdetection of COVID-19 cases in France threatens epidemic control

Abstract

As countries in Europe gradually relaxed lockdown restrictions after the first wave, test-trace-isolate strategies became critical to maintain COVID-19 viral activity at low levels. Reviewing their shortcomings can provide elements to consider in light of the second wave currently underway in Europe. Here we estimate the rate of detection of COVID-19 symptomatic cases in France after lockdown through the use of virological and participatory syndromic surveillance data coupled with mathematical transmission models calibrated to regional hospitalizations. Our findings indicate that around 90,000 incident symptomatic infections, corresponding to 9 out 10 cases, were not ascertained by the

surveillance system in the first 7 weeks following lockdown from May 11 to June 28 2020, although the test positivity rate did not exceed WHO recommendations (5%). The median detection rate increased from 7% [6-8]% to 38% [35-44]% over time, with large regional variations, owing to a strengthening of the system as well as a decrease of epidemic activity. According to participatory surveillance data, only 31% of individuals with COVID-19-like symptoms consulted a doctor in the study period. This suggests that large numbers of symptomatic COVID-19 cases did not seek medical advice despite recommendations, as confirmed by serological studies. Encouraging awareness and same-day healthcare-seeking behavior in suspect cases is critical to improve detection. However, the capacity of the system remained insufficient even at the low levels of viral circulation achieved after lockdown, and was predicted to deteriorate rapidly with increasing epidemic activity. Substantially more aggressive, targeted, and efficient testing with easier access is required to act as a pandemic-fighting tool. Testing strategy will be once again of critical value to lift current restrictive measures in Europe and avoid a third wave.

Reference

https://www.nature.com/articles/s41586-020-03095-6

Genomic epidemiology reveals multiple introductions of SARS-CoV-2 from mainland Europe into Scotland

Abstract

Coronavirus disease 2019 (COVID-19) was first diagnosed in Scotland on 1 March 2020. During the first month of the outbreak, 2,641 cases of COVID-19 led to 1,832 hospital admissions, 207 intensive care admissions and 126 deaths. We aimed to identify the source and number of introductions of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) into Scotland using a combined phylogenetic and epidemiological approach. Sequencing of 1,314 SARS-CoV-2 viral genomes from available patient samples enabled us to estimate that SARS-CoV-2 was introduced to Scotland on at least 283 occasions during February and March 2020. Epidemiological analysis confirmed that early introductions of SARS-CoV-2 originated from mainland Europe (the majority from Italy and Spain). We identified subsequent early outbreaks in the community, within

healthcare facilities and at an international conference. Community transmission occurred after 2 March, 3 weeks before control measures were introduced. Earlier travel restrictions or quarantine measures, both locally and internationally, would have reduced the number of COVID-19 cases in Scotland. The risk of multiple reintroduction events in future waves of infection remains high in the absence of population immunity.

Reference

https://www.nature.com/articles/s41564-020-00838-z

Multiplex assays for the identification of serological signatures of SARS-CoV-2 infection: An antibody-based diagnostic and machine learning study

Abstract

Background: Infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) induces an antibody response targeting multiple antigens that changes over time. This study aims to take advantage of this complexity to develop more accurate serological diagnostics.

Methods: A multiplex serological assay was developed to measure IgG and IgM antibody responses to seven SARS-CoV-2 spike or nucleoprotein antigens, two antigens for the nucleoproteins of the 229E and NL63 seasonal coronaviruses, and three non-coronavirus antigens. Antibodies were measured in serum samples collected up to 39 days after symptom onset from 215 adults in four French hospitals (53 patients and 162 health-care workers) with quantitative RT-PCR-confirmed SARS-CoV-2 infection, and negative control serum samples collected from healthy adult blood donors before the start of the SARS-CoV-2 epidemic (335 samples from France, Thailand, and Peru). Machine learning classifiers were trained with the multiplex data to classify individuals with previous SARS-CoV-2 infection, with the best classification performance displayed by a random forests algorithm. A Bayesian mathematical model of antibody kinetics informed by prior information from other coronaviruses was used to estimate time-varying antibody responses and assess the sensitivity and classification performance of serological diagnostics during the first year following symptom onset. A statistical estimator is presented that can provide estimates of seroprevalence in very low-transmission settings.

Findings: IgG antibody responses to trimeric spike protein (Stri) identified individuals with previous SARS-CoV-2 infection with 91·6% (95% CI 87·5–94·5) sensitivity and 99·1% (97·4–99·7) specificity. Using a serological signature of IgG and IgM to multiple antigens, it was possible to identify infected individuals with 98·8% (96·5–99·6) sensitivity and 99·3% (97·6–99·8) specificity. Informed by existing data from other coronaviruses, we estimate that 1 year after infection, a monoplex assay with optimal anti-Stri IgG cutoff has 88·7% (95% credible interval 63·4–97·4) sensitivity and that a four-antigen multiplex assay can increase sensitivity to 96·4% (80·9–100·0). When applied to population-level serological surveys, statistical analysis of multiplex data allows estimation of seroprevalence levels less than 2%, below the false-positivity rate of many other assays.

Interpretation: Serological signatures based on antibody responses to multiple antigens can provide accurate and robust serological classification of individuals with previous SARS-CoV-2 infection. This provides potential solutions to two pressing challenges for SARS-CoV-2 serological surveillance: classifying individuals who were infected more than 6 months ago and measuring seroprevalence in serological surveys in very low-transmission settings.

Reference

https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247(20)30197-X/fulltext

Publication Date: Dec 19, 2020

Dysregulation of cell signaling by SARS-CoV-2

Abstract

Pathogens usurp host pathways to generate a permissive environment for their propagation. The current spread of Severe Acute Respiratory Syndrome coronavirus-2 (SARS-CoV-2) infection presents the urgent need to understand the complex pathogen-host interplay for effective control of the virus. SARS-CoV-2 reorganizes the host cytoskeleton for efficient cell entry and controls host transcriptional processes to support viral protein translation. The virus also dysregulates innate cellular defenses using various structural and nonstructural proteins. This results in substantial but delayed hyperinflammation alongside a weakened interferon response. We provide an overview

of SARS-CoV-2 and its uniquely aggressive lifecycle and discuss the interactions of various viral proteins with host signaling pathways. We also address the functional changes in SARS-CoV-2 proteins, relative to SARS-CoV. Our comprehensive assessment of host signaling in SARS-CoV-2 pathogenesis provides some complex yet important strategic clues for the development of novel therapeutics against this rapidly emerging worldwide crisis.

Reference

https://www.cell.com/trends/microbiology/fulltext/S0966-842X(20)30324-3

Publication Date: Dec 18, 2020

Viral targets for vaccines against COVID-19

Abstract

Vaccines are urgently needed to control the coronavirus disease 2019 (COVID-19) pandemic and to help the return to pre-pandemic normalcy. A great many vaccine candidates are being developed, several of which have completed late-stage clinical trials and are reporting positive results. In this Progress article, we discuss which viral elements are used in COVID-19 vaccine candidates, why they might act as good targets for the immune system and the implications for protective immunity.

Reference

https://www.nature.com/articles/s41577-020-00480-0

The diagnostic accuracy of isothermal nucleic acid point-of-care tests for human coronaviruses: A systematic review and meta-analysis

Abstract

Many recent studies reported coronavirus point-of-care tests (POCTs) based on isothermal amplification. However, the performances of these tests have not been systematically evaluated. Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy was used as a guideline for conducting this systematic review. We searched peer-reviewed and preprint articles in PubMed, BioRxiv and MedRxiv up to 28 September

2020 to identify studies that provide data to calculate sensitivity, specificity and diagnostic odds ratio (DOR). Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) was applied for assessing quality of included studies and Preferred Reporting Items for a Systematic Review and Meta-analysis of Diagnostic Test Accuracy Studies (PRISMA-DTA) was followed for reporting. We included 81 studies from 65 research articles on POCTs of SARS, MERS and COVID-19. Most studies had high risk of patient selection and index test bias but low risk in other domains. Diagnostic specificities were high (> 0.95) for included studies while sensitivities varied depending on type of assays and sample used. Most studies (n = 51) used reverse transcription loop-mediated isothermal amplification (RT-LAMP) to diagnose coronaviruses. RT-LAMP of RNA purified from COVID-19 patient samples had pooled sensitivity at 0.94 (95% CI: 0.90–0.96). RT-LAMP of crude samples had substantially lower sensitivity at 0.78 (95% CI: 0.65–0.87). Abbott ID Now performance was similar to RT-LAMP of crude samples. Diagnostic performances by CRISPR and RT-LAMP on purified RNA were similar. Other diagnostic platforms including RT- recombinase assisted amplification (RT-RAA) and SAMBA-II also offered high sensitivity (> 0.95). Future studies should focus on the use of un-bias patient cohorts, double-blinded index test and detection assays that do not require RNA extraction.

Reference

https://www.nature.com/articles/s41598-020-79237-7

Dynamic data-driven meta-analysis for prioritisation of host genes implicated in COVID-19

Abstract

The increasing body of literature describing the role of host factors in COVID-19 pathogenesis demonstrates the need to combine diverse, multi-omic data to evaluate and substantiate the most robust evidence and inform development of therapies. Here we present a dynamic ranking of host genes implicated in human betacoronavirus infection (SARS-CoV-2, SARS-CoV, MERS-CoV, seasonal coronaviruses). We conducted an extensive systematic review of experiments identifying potential host factors. Gene lists from diverse sources were integrated using Meta-Analysis by Information Content (MAIC). This previously described algorithm uses data-driven gene list weightings to

produce a comprehensive ranked list of implicated host genes. From 32 datasets, the top ranked gene was PPIA, encoding cyclophilin A, a druggable target using cyclosporine. Other highly-ranked genes included proposed prognostic factors (CXCL10, CD4, CD3E) and investigational therapeutic targets (IL1A) for COVID-19. Gene rankings also inform the interpretation of COVID-19 GWAS results, implicating FYCO1 over other nearby genes in a disease-associated locus on chromosome 3. Researchers can search and review the gene rankings and the contribution of different experimental methods to gene rank at https://baillielab.net/maic/covid19. As new data are published we will regularly update the list of genes as a resource to inform and prioritise future studies.

Reference

https://www.nature.com/articles/s41598-020-79033-3

Publication Date: Dec 17, 2020

Phase 1/2 trial of SARS-CoV-2 vaccine ChAdOx1 nCoV-19 with a booster dose induces multifunctional antibody responses

Abstract

More than 190 vaccines are currently in development to prevent infection by the novel severe acute respiratory syndrome coronavirus 2. Animal studies suggest that while neutralizing antibodies against the viral spike protein may correlate with protection, additional antibody functions may also be important in preventing infection. Previously, we reported early immunogenicity and safety outcomes of a viral vector coronavirus vaccine, ChAdOx1 nCoV-19 (AZD1222), in a single-blinded phase 1/2 randomized controlled trial of healthy adults aged 18–55 years (NCT04324606). Now we describe safety and exploratory humoral and cellular immunogenicity of the vaccine, from subgroups of volunteers in that trial, who were subsequently allocated to receive a homologous full-dose (SD/SD D56; n = 20) or half-dose (SD/LD D56; n = 32) ChAdOx1 booster vaccine 56 d following prime vaccination. Previously reported immunogenicity data from the open-label 28-d interval prime-boost group (SD/SD D28; n = 10) are also presented to facilitate comparison. Additionally, we describe volunteers boosted with the comparator vaccine (MenACWY; n = 10). In this interim report, we demonstrate that a booster dose of ChAdOx1 nCoV-19 is safe and better tolerated than priming doses. Using

a systems serology approach we also demonstrate that anti-spike neutralizing antibody titers, as well as Fc-mediated functional antibody responses, including antibody-dependent neutrophil/monocyte phagocytosis, complement activation and natural killer cell activation, are substantially enhanced by a booster dose of vaccine. A booster dose of vaccine induced stronger antibody responses than a dose-sparing half-dose boost, although the magnitude of T cell responses did not increase with either boost dose. These data support the two-dose vaccine regime that is now being evaluated in phase 3 clinical trials.

Reference

https://www.nature.com/articles/s41591-020-01179-4

CoV2-ID, a MIQE-compliant sub-20-min 5-plex RT-PCR assay targeting SARS-CoV-2 for the diagnosis of COVID-19

Abstract

Accurate, reliable and rapid detection of SARS-CoV-2 is essential not only for correct diagnosis of individual COVID-19 disease but also for the development of a rational strategy aimed at lifting confinement restrictions and preparing for possible recurrent waves of viral infections. We have used the MIQE guidelines to develop two versions of a unique five plex RT-qPCR test, termed CoV2-ID, that allows the detection of three viral target genes, a human internal control for confirming the presence of human cells in a sample and a control artificial RNA for quality assessment and potential quantification. Viral targets can be detected either individually with separate fluorophores or jointly using the same fluorophore, thus increasing the test's reliability and sensitivity. It is robust, can consistently detect two copies of viral RNA, with a limit of detection of a single copy and can be completed in around 15 min. It was 100% sensitive and 100% specific when tested on 23 RNA samples extracted from COVID-19 positive patients and five COVID-19 negative patients. We also propose using multiple cycle fluorescence detection, rather than real-time PCR to reduce significantly the time taken to complete the assay as well as assuage the misunderstandings underlying the use of quantification cycles (Cq). Finally, we have designed an assay for the detection of the D614G mutation and show that all of the samples isolated in the Chelmsford, Essex area between mid-April and June

2020, have the mutant genotype whereas a sample originating in Australia was infected with the wild type genotype.

Reference

https://www.nature.com/articles/s41598-020-79233-x

Biochemical and biophysical characterization of the main protease, 3-chymotrypsin-like protease (3CLpro) from the novel coronavirus SARS-CoV 2

Abstract

Severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2) is responsible for the novel coronavirus disease 2019 (COVID-19). An appealing antiviral drug target is the coronavirus 3C-like protease (3CLpro) that is responsible for the processing of the viral polyproteins and liberation of functional proteins essential for the maturation and infectivity of the virus. In this study, multiple thermal analytical techniques have been implemented to acquire the thermodynamic parameters of 3CLpro at different buffer conditions. 3CLpro exhibited relatively high thermodynamic stabilities over a wide pH range; however, the protease was found to be less stable in the presence of salts. Divalent metal cations reduced the thermodynamic stability of 3CLpro more than monovalent cations; however, altering the ionic strength of the buffer solution did not alter the stability of 3CLpro. Furthermore, the most stable thermal kinetic stability of 3CLpro was recorded at pH 7.5, with the highest enthalpy of activation calculated from the slope of Eyring plot. The biochemical and biophysical properties of 3CLpro explored here may improve the solubility and stability of 3CLpro for optimum conditions for the setup of an enzymatic assay for the screening of inhibitors to be used as lead candidates in the discovery of drugs and design of antiviral therapeutics against COVID-19.

Reference

https://www.nature.com/articles/s41598-020-79357-0

T cell and antibody responses induced by a single dose of ChAdOx1 nCoV-19 (AZD1222) vaccine in a phase 1/2 clinical trial

Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative agent of Coronavirus Disease 2019 (COVID-19), has caused a global pandemic, and safe, effective vaccines are urgently needed1. Strong, Th1-skewed T cell responses can drive protective humoral and cell-mediated immune responses2 and might reduce the potential for disease enhancement3. Cytotoxic T cells clear virus-infected host cells and contribute to control of infection4. Studies of patients infected with SARS-CoV-2 have suggested a protective role for both humoral and cell-mediated immune responses in recovery from COVID-19 (refs. 5,6). ChAdOx1 nCoV-19 (AZD1222) is a candidate SARS-CoV-2 vaccine comprising a replication-deficient simian adenovirus expressing full-length SARS-CoV-2 spike protein. We recently reported preliminary safety and immunogenicity data from a phase 1/2 trial of the ChAdOx1 nCoV-19 vaccine (NCT04400838)7 given as either a one- or two-dose regimen. The vaccine was tolerated, with induction of neutralizing antibodies and antigen-specific T cells against the SARS-CoV-2 spike protein. Here we describe, in detail, exploratory analyses of the immune responses in adults, aged 18–55 years, up to 8 weeks after vaccination with a single dose of ChAdOx1 nCoV-19 in this trial, demonstrating an induction of a Th1-biased response characterized by interferon-γ and tumor necrosis factor-α cytokine secretion by CD4+ T cells and antibody production predominantly of IgG1 and IgG3 subclasses. CD8+ T cells, of monofunctional, polyfunctional and cytotoxic phenotypes, were also induced. Taken together, these results suggest a favorable immune profile induced by ChAdOx1 nCoV-19 vaccine, supporting the progression of this vaccine candidate to ongoing phase 2/3 trials to assess vaccine efficacy.

Reference

https://www.nature.com/articles/s41591-020-01194-5

COVID-19 cycles and rapidly evaluating lockdown strategies using spectral analysis

Abstract

Spectral analysis characterises oscillatory time series behaviours such as cycles, but accurate estimation requires reasonable numbers of observations. At the time of writing, COVID-19 time series for many countries are short: pre- and post-lockdown series are shorter still. Accurate estimation of potentially interesting cycles seems beyond reach with such short series. We solve the problem of obtaining accurate estimates from short series by using recent Bayesian spectral fusion methods. We show that transformed daily COVID-19 cases for many countries generally contain three cycles operating at wavelengths of around 2.7, 4.1 and 6.7 days (weekly) and that shorter wavelength cycles are suppressed after lockdown. The pre- and post-lockdown differences suggest that the weekly effect is at least partly due to non-epidemic factors. Unconstrained, new cases grow exponentially, but the internal cyclic structure causes periodic declines. This suggests that lockdown success might only be indicated by four or more daily falls. Spectral learning for epidemic time series contributes to the understanding of the epidemic process and can help evaluate interventions. Spectral fusion is a general technique that can fuse spectra recorded at different sampling rates, which can be applied to a wide range of time series from many disciplines.

Reference

https://www.nature.com/articles/s41598-020-79092-6

Exploring the effectiveness of a COVID-19 contact tracing app using an agent-based model

A contact-tracing strategy has been deemed necessary to contain the spread of COVID-19 following the relaxation of lockdown measures. Using an agent-based model, we explore one of the technology-based strategies proposed, a contact-tracing smartphone app. The model simulates the spread of COVID-19 in a population of agents on an urban scale. Agents are heterogeneous in their characteristics and are linked in a multi-layered network representing the social structure—including households, friendships, employment and schools. We explore the interplay of various adoption rates of the

contact-tracing app, different levels of testing capacity, and behavioural factors to assess the impact on the epidemic. Results suggest that a contact tracing app can contribute substantially to reducing infection rates in the population when accompanied by a sufficient testing capacity or when the testing policy prioritises symptomatic cases. As user rate increases, prevalence of infection decreases. With that, when symptomatic cases are not prioritised for testing, a high rate of app users can generate an extensive increase in the demand for testing, which, if not met with adequate supply, may render the app counterproductive. This points to the crucial role of an efficient testing policy and the necessity to upscale testing capacity.

Reference

https://www.nature.com/articles/s41598-020-79000-y

A systematic review and meta-analysis on chloroquine and hydroxychloroquine as monotherapy or combined with azithromycin in COVID-19 treatment

Abstract

Many recent studies have investigated the role of either Chloroquine (CQ) or Hydroxychloroquine (HCQ) alone or in combination with azithromycin (AZM) in the management of the emerging coronavirus. This systematic review and meta-analysis of either published or preprint observational studies or randomized control trials (RCT) aimed to assess mortality rate, duration of hospital stay, need for mechanical ventilation (MV), virologic cure rate (VQR), time to a negative viral polymerase chain reaction (PCR), radiological progression, experiencing drug side effects, and clinical worsening. A search of the online database through June 2020 was performed and examined the reference lists of pertinent articles for in-vivo studies only. Pooled relative risks (RRs), standard mean differences of 95% confidence intervals (CIs) were calculated with the random-effects model. Mortality was not different between the standard care (SC) and HCQ groups (RR = 0.99, 95% CI 0.61–1.59, I2 = 82%), meta-regression analysis proved that mortality was significantly different across the studies from different countries. However, mortality among the HCQ + AZM was significantly higher than among the SC (RR = 1.8, 95% CI 1.19–2.27, I2 = 70%). The duration of hospital stay in days was shorter in the SC in comparison with the HCQ group (standard mean difference = 0.57, 95% CI 0.20–0.94, I2 = 92%), or the HCQ + AZM (standard mean difference = 0.77, 95% CI 0.46–1.08,

I2 = 81). Overall VQR, and that at days 4, 10, and 14 among patients exposed to HCQ did not differ significantly from the SC [(RR = 0.92, 95% CI 0.69–1.23, I2 = 67%), (RR = 1.11, 95% CI 0.26–4.69, I2 = 85%), (RR = 1.21, 95% CI 0.70–2.01, I2 = 95%), and (RR = 0.98, 95% CI 0.76–1.27, I2 = 85%)] respectively. Exposure to HCQ + AZM did not improve the VQR as well (RR = 3.23, 95% CI 0.70–14.97, I2 = 58%). The need for MV was not significantly different between the SC and HCQ (RR = 1.5, 95% CI 0.78–2.89, I2 = 81%), or HCQ + AZM (RR = 1.27, 95% CI 0.7–2.13, I2 = 88%). Side effects were more reported in the HCQ group than in the SC (RR = 3.14, 95% CI 1.58–6.24, I2 = 0). Radiological improvement and clinical worsening were not statistically different between HCQ and SC [(RR = 1.11, 95% CI 0.74–1.65, I2 = 45%) and (RR = 1.28, 95% CI 0.33–4.99), I2 = 54%] respectively. Despite the scarcity of published data of good quality, the effectiveness and safety of either HCQ alone or in combination with AZM in treating COVID-19 cannot be assured. Future high-quality RCTs need to be carried out.

Reference

https://www.nature.com/articles/s41598-020-77748-x

A report on COVID-19 epidemic in Pakistan using SEIR fractional model

Abstract

Recently, novel coronavirus is a serious global issue and having a negative impact on the economy of the whole world. Like other countries, it also effected the economy and people of Pakistan. According to the publicly reported data, the first case of novel corona virus in Pakistan was reported on 27th February 2020. The aim of the present study is to describe the mathematical model and dynamics of COVID-19 in Pakistan. To investigate the spread of coronavirus in Pakistan, we develop the SEIR time fractional model with newly, developed fractional operator of Atangana–Baleanu. We present briefly the analysis of the given model and discuss its applications using world health organization (WHO) reported data for Pakistan. We consider the available infection cases from 19th March 2020, till 31st March 2020 and accordingly, various parameters are fitted or estimated. It is worth noting that we have calculated the basic reproduction number {\mathfrak{R}}_{0} \approx 2.30748 which shows that virus is spreading rapidly. Furthermore, stability analysis of the model at disease free equilibrium DFE and endemic equilibriums EE is

performed to observe the dynamics and transmission of the model. Finally, the AB fractional model is solved numerically. To show the effect of the various embedded parameters like fractional parameter \alpha on the model, various graphs are plotted. It is worth noting that the base of our investigation, we have predicted the spread of disease for next 200 days.

Reference

https://www.nature.com/articles/s41598-020-79405-9

Renin–angiotensin system blockers and susceptibility to COVID-19: An international, open science, cohort analysis

Abstract

Background: Angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) have been postulated to affect susceptibility to COVID-19. Observational studies so far have lacked rigorous ascertainment adjustment and international generalisability. We aimed to determine whether use of ACEIs or ARBs is associated with an increased susceptibility to COVID-19 in patients with hypertension.

Methods: In this international, open science, cohort analysis, we used electronic health records from Spain (Information Systems for Research in Primary Care [SIDIAP]) and the USA (Columbia University Irving Medical Center data warehouse [CUIMC] and Department of Veterans Affairs Observational Medical Outcomes Partnership [VA-OMOP]) to identify patients aged 18 years or older with at least one prescription for ACEIs and ARBs (target cohort) or calcium channel blockers (CCBs) and thiazide or thiazide-like diuretics (THZs; comparator cohort) between Nov 1, 2019, and Jan 31, 2020. Users were defined separately as receiving either monotherapy with these four drug classes, or monotherapy or combination therapy (combination use) with other antihypertensive medications. We assessed four outcomes: COVID-19 diagnosis; hospital admission with COVID-19; hospital admission with pneumonia; and hospital admission with pneumonia, acute respiratory distress syndrome, acute kidney injury, or sepsis. We built large-scale propensity score methods derived through a data-driven approach and negative control experiments across ten pairwise comparisons, with results meta-analysed to generate 1280 study effects. For each study effect, we did negative control outcome experiments

using a possible 123 controls identified through a data-rich algorithm. This process used a set of predefined baseline patient characteristics to provide the most accurate prediction of treatment and balance among patient cohorts across characteristics. The study is registered with the EU Post-Authorisation Studies register, EUPAS35296.

Reference

https://www.thelancet.com/journals/landig/article/PIIS2589-7500(20)30289-2/fulltext

Comparison of the characteristics, morbidity, and mortality of COVID-19 and seasonal influenza: A nationwide, population-based retrospective cohort study

Abstract

Background: To date, influenza epidemics have been considered suitable for use as a model for the COVID-19 epidemic, given that they are respiratory diseases with similar modes of transmission. However, data directly comparing the two diseases are scarce.

Methods: We did a nationwide retrospective cohort study using the French national administrative database (PMSI), which includes discharge summaries for all hospital admissions in France. All patients hospitalised for COVID-19 from March 1 to April 30, 2020, and all patients hospitalised for influenza between Dec 1, 2018, and Feb 28, 2019, were included. The diagnosis of COVID-19 (International Classification of Diseases [10th edition] codes U07.10, U07.11, U07.12, U07.14, or U07.15) or influenza (J09, J10, or J11) comprised primary, related, or associated diagnosis. Comparisons of risk factors, clinical characteristics, and outcomes between patients hospitalised for COVID-19 and influenza were done, with data also stratified by age group.

Findings: 89 530 patients with COVID-19 and 45 819 patients with influenza were hospitalised in France during the respective study periods. The median age of patients was 68 years (IQR 52–82) for COVID-19 and 71 years (34–84) for influenza. Patients with COVID-19 were more frequently obese or overweight, and more frequently had diabetes, hypertension, and dyslipidaemia than patients with influenza, whereas those with influenza more frequently had heart failure, chronic respiratory disease, cirrhosis, and deficiency anaemia. Patients admitted to hospital with COVID-19 more frequently developed acute respiratory failure, pulmonary embolism, septic shock, or haemorrhagic

stroke than patients with influenza, but less frequently developed myocardial infarction or atrial fibrillation. In-hospital mortality was higher in patients with COVID-19 than in patients with influenza (15 104 [16·9%] of 89 530 vs 2640 [5·8%] of 45 819), with a relative risk of death of 2·9 (95% CI 2·8–3·0) and an age-standardised mortality ratio of 2·82. Of the patients hospitalised, the proportion of paediatric patients (<18 years) was smaller for COVID-19 than for influenza (1227 [1·4%] vs 8942 [19·5%]), but a larger proportion of patients younger than 5 years needed intensive care support for COVID-19 than for influenza (14 [2·3%] of 613 vs 65 [0·9%] of 6973). In adolescents (11–17 years), the in-hospital mortality was ten-times higher for COVID-19 than for influenza (five [1·1% of 458 vs one [0·1%] of 804), and patients with COVID-19 were more frequently obese or overweight.

Interpretation: The presentation of patients with COVID-19 and seasonal influenza requiring hospitalisation differs considerably. Severe acute respiratory syndrome coronavirus 2 is likely to have a higher potential for respiratory pathogenicity, leading to more respiratory complications and to higher mortality. In children, although the rate of hospitalisation for COVID-19 appears to be lower than for influenza, in-hospital mortality is higher; however, low patient numbers limit this finding. These findings highlight the importance of appropriate preventive measures for COVID-19, as well as the need for a specific vaccine and treatment.

Reference

https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30527-0/fulltext

Renin–angiotensin system inhibitors and COVID-19: Overwhelming evidence against an association

Abstract

Inhibitors of the renin–angiotensin system (RAS) have been reported to increase the expression of angiotensin-converting enzyme 2 (ACE2) in animal models. This possibility, along with the high prevalence of cardiovascular diseases (for which RAS inhibitors are often used) among patients with severe COVID-19 prompted some researchers to postulate that these drugs could enhance the access of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) into cells, predisposing patients to COVID-19 or

progression to more severe forms. This hypothesis was widely publicised in mid-March, 2020, coinciding with the surge of the first pandemic wave in Europe, and many physicians faced an awful dilemma: to withdraw or not to withdraw these drugs, with the implicit harms of either decision. Scientific societies and regulatory authorities counteracted by recommending not to discontinue RAS inhibitors until firm evidence was available and urged investigators worldwide to carry out studies to test the hypothesis. In less than 2 months, three large studies, from different countries and using diverse designs, were published, reaching the same conclusion: the absence of an association of RAS inhibitors with COVID-19 diagnosis, hospital admission, and severity, which provided a first reassurance on the safety of these drugs. Since then, more than 50 studies have been published, with the same conclusion. However, many of them were small, single centred, and methodologically weak.

Reference

https://www.thelancet.com/journals/landig/article/PIIS2589-7500(20)30294-6/fulltext

Publication Date: Dec 22, 2020

Compromised SARS-CoV-2-specific placental antibody transfer

Abstract

SARS-CoV-2 infection causes more severe disease in pregnant women compared to age-matched non-pregnant women. Whether maternal infection causes changes in the transfer of immunity to infants remains unclear. Maternal infections have previously been associated with compromised placental antibody transfer, but the mechanism underlying this compromised transfer is not established. Here, we used systems serology to characterize the Fc-profile of influenza-, pertussis-, and SARS-CoV-2-specific antibodies transferred across the placenta. Influenza- and pertussis-specific antibodies were actively transferred. However, SARS-CoV-2-specific antibody transfer was significantly reduced compared to influenza- and pertussis-specific antibodies, and cord titers and functional activity were lower than in maternal plasma. This effect was only observed in third trimester infection. SARS-CoV-2-specific transfer was linked to altered SARS-CoV-2-antibody glycosylation profiles and was partially rescued by infection-induced increases in IgG and increased FCGR3A placental expression. These results point to unexpected

compensatory mechanisms to boost immunity in neonates, providing insights for maternal vaccine design.

Reference

https://www.sciencedirect.com/science/article/pii/S0092867420317499

PERSPECTIVE

Publication Date: Dec 18, 2020

The assessment of convalescent plasma efficacy against COVID-19

Antibody-based therapy for infectious diseases predates modern antibiotics and, in the absence of other therapeutic options, was deployed early in the SARS-CoV-2 pandemic through COVID-19 convalescent plasma (CCP) administration. Although most studies have demonstrated signals of efficacy for CCP, definitive assessment has proved difficult under pandemic conditions, with rapid changes in disease incidence and the knowledge base complicating the design and implementation of randomized controlled trials. Nevertheless, evidence from a variety of studies demonstrates that CCP is as safe as ordinary plasma and strongly suggests that it can reduce mortality if given early and with sufficient antibody content.

The coronavirus disease 2019 (COVID-19) pandemic in 2020, a catastrophic event in human history, led to rapid mobilization of the biomedical research establishment to find both preventive and therapeutic options. The causative agent, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), posed a major challenge because, as a new virus, it had no specific preexisting therapy. Consequently, early responses focused on optimizing respiratory care, managing thrombotic and inflammatory complications with anticoagulation and corticosteroids, and repurposing existing antiviral therapies, which, with the exception of remdesivir, proved ineffective. Another approach, in the desperate early days of the pandemic, was the revival of convalescent plasma (CP), an old therapy dating back to the early 20th century. CP was used with apparent success in numerous epidemics and outbreaks, including the 1918 influenza pandemic, and was proposed as a strategy for new pandemics a decade ago. The premise for this therapeutic approach is that CP transfers specific antibodies made by individuals who have recovered from COVID-19 to people at risk for, or suffering from, this disease.

First used against SARS-CoV-2 in China and Italy, COVID-19 CP (CCP) was rapidly deployed in many countries, including the United States, where more than 85,000 patients had been treated with CP as of late August 2020. The extensive use of CCP in the United States occurred after the U.S. Food and Drug Administration (FDA) allowed plasma

administration to COVID-19 patients under three successive regulatory mechanisms. The first, issued in late March 2020, authorized case-by-case compassionate use upon physician request. Shortly thereafter, in early April, an expanded access program (EAP) permitted physicians to treat patients who were, or were at risk for becoming, critically ill with COVID-19 under the condition that they register their patients in a Biomedical Advanced Research and Development Authority (BARDA)-funded single-arm national observational study administered by the Mayo Clinic. The third step took place on August 23, when the FDA reviewed the safety and efficacy data generated by the EAP and authorized treatment of hospitalized patients with CCP as long as a national state of emergency existed, a step called an emergency use authorization (EUA). CCP and remdesivir are currently the only two treatments for COVID-19 patients that have received FDA EUA. Remdesivir received FDA approval on October 22, 2020.

Although sometimes seen as a bridge to other antibody-based therapies such as monoclonal antibodies (mAbs) and hyperimmune globulins, CCP established a definite presence in the therapeutic arsenal against COVID-19 early in the pandemic. In the months that followed the FDA's EAP issuance, CCP use increased beyond expectations, leading to criticism that this modality was being deployed clinically without sufficiently rigorous efficacy trials. In this perspective, we review how CCP emerged as a leading COVID-19 therapy and consider the issues encountered in establishing its efficacy, with particular emphasis on the unique complexities involved in conducting randomized clinical trials with a heterogeneous product during a pandemic with limited information on the conditions for ideal use. For more details, read the link given below.

Reference

https://www.cell.com/med/fulltext/S2666-6340(20)30025-8

NEWSLETTER

Publication Date: Dec 18, 2020

Moderna COVID vaccine becomes second to get US authorization

Moderna's vaccine, which was developed in collaboration with the US National Institute of Allergy and Infectious Diseases, works in the same way as the one produced by Pfizer and BioNTech. Both consist of RNA molecules encased in lipid nanoparticles. The RNA in both vaccines encodes a slightly modified form of the SARS-CoV-2 protein known as spike, which enables the virus to infect human cells. Once taken up by cells, the RNA is used to produce the protein, which then triggers an immune response. The RNA does not enter the nucleus where the cell's genome resides, and is degraded by the cell within a day of the injection.

Like Pfizer's vaccine, Moderna's seems to be highly effective — about 94% — at preventing symptomatic SARS-CoV-2 infections. Its safety profile is also similar to Pfizer's, with fatigue, headaches and pain at the site of injection among the most often cited side effects.

The two vaccines differ in the composition of the lipid nanoparticle that encases the RNA, and Moderna's formulation allows the vaccine to be stored at higher temperature than Pfizer's, which must be kept at −70 °C, much colder than a normal freezer. Moderna's vaccine can be stored in a −20 °C freezer for 6 months, and in a refrigerator (at about 4 °C) for 30 days. This promises to streamline the logistics of deploying the vaccine, particularly in rural areas and in countries with limited health-care infrastructure.

Reference

https://www.nature.com/articles/d41586-020-03593-7

FORUM

Publication Date: Dec 21, 2020

Biosensing detection of the SARS-CoV-2 D614G mutation

The emergence of a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) mutant virus with an amino acid change from aspartate to a glycine residue at position 614 (D614G) has been reported and this mutant appears to be now dominant in the pandemic. Efficient detection of the SARS-CoV-2 D614G mutant by biosensing technologies is therefore crucial for the control of the pandemic. For more details, read the link given below.

Reference

https://www.cell.com/trends/genetics/fulltext/S0168-9525(20)30334-6

Animal Behavioral Responses to the COVID-19 Quietus

Lockdown measures fundamentally reshaped human society during the COVID-19 pandemic. We present a framework featuring seven animal behavioral changes to the calming effect of the lockdowns on human actions (COVID-19 quietus). We demonstrate how this framework can be used to quantify animal behavioral responses with implications for ecology and conservation. For more details, read the link given below.

Reference

https://www.cell.com/trends/ecology-evolution/fulltext/S0169-5347(20)30371-2

OPINION

Publication Date: Dec 19, 2020

Emerging role for MAIT cells in control of antimicrobial resistance

Host immunity is an important factor in clearing antibiotic-resistant bacterial infections that is often neglected. Understanding host immunity can provide novel insights for alternative intervention strategies against antimicrobial resistance.

Mucosa-associated invariant T (MAIT) cells are key players in human antibacterial immunity. These highly abundant unconventional T cells recognise by-products from bacterial vitamin B2 biosynthesis, and mediate bacterial control through direct killing and orchestrating downstream immune responses.

MAIT cells have the capacity to control drug-resistant bacteria and overcome resistance. This suggests that MAIT cells may participate in the clearance of bacteria that acquire resistance during antibiotic therapy and may provide protection against infections by resistant bacteria. Enhancing MAIT cell properties may be a viable prophylaxis and alternative treatment strategy in vulnerable populations.

Antimicrobial resistance is a serious threat to global public health as antibiotics are losing effectiveness due to rapid development of resistance. The human immune system facilitates control and clearance of resistant bacterial populations during the course of antimicrobial therapy. Here we review current knowledge of mucosa-associated invariant T (MAIT) cells, an arm of the immune system on the border between innate and adaptive, and their critical place in human antibacterial immunity. We propose that MAIT cells play important roles against antimicrobial-resistant infections through their capacity to directly clear multidrug-resistant bacteria and overcome mechanisms of antimicrobial resistance. Finally, we discuss outstanding questions pertinent to the possible advancement of host-directed therapy as an alternative intervention strategy for antimicrobial-resistant bacterial infections.

Reference

https://www.cell.com/trends/microbiology/fulltext/S0966-842X(20)30314-0

PREVIEW

Publication Date: Dec 17, 2020

A crisp(r) new perspective on SARS-CoV-2 biology

Complementary genome-wide CRISPR-Cas9 screens performed by multiple groups reveal new insights into SARS-CoV-2 biology including aspects of viral entry, translation, replication, egress, and the genes regulating these processes. Comparisons with other coronaviruses enhances our understanding of the cellular life cycle of this medically important family of emerging viruses. For more details, read the link given below.

Reference

https://www.cell.com/cell/fulltext/S0092-8674(20)31625-1

COMMENTARY

Publication Date: Dec 23, 2020

Observational research on severe COVID-19 in diabetes

Older age is by far the strongest risk factor for severe COVID-19, followed by deprivation, non-white ethnicity, male sex, and chronic medical conditions. Such information can guide protection and vaccination strategies, and can provide leads for causal inference and development of novel treatments. However, in seeking to define risk factors for severe COVID-19, scientific thoroughness has often lost out to superficial newsworthiness. There has been a huge increase in the use of preprint servers, with media coverage preceding peer review and unparallelled fast-tracking of COVID-19 reports. Many reports have lacked careful epidemiologic design, conduct, and analysis. For example, many small studies with few clinical events have reported strong associations that—in view of unavoidable publication bias—are likely to be spurious. Additionally, hospitalisation and critical care unit admission are biased markers of severe COVID-19 because they are subject to hospitalisation and critical care unit admission policies. For more details, read the link given below.

Reference

https://www.thelancet.com/journals/landia/article/PIIS2213-8587(20)30432-0/fulltext

Publication Date: Dec 18, 2020

Vaccination is the only acceptable path to herd immunity

Population-level herd immunity is critical for long-term control of SARS-CoV-2. However, proposals to reach the herd immunity threshold through naturally acquired infection, rather than vaccination, have complicated public health efforts and popularized policies that will lead to widespread transmission and mortality. Vaccination is the only viable path to herd immunity. For more details, read the link given below.

Reference

https://www.cell.com/med/fulltext/S2666-6340(20)30032-5