RESEARCH PUBLICATIONS

Publication Date: Mar 24, 2021

Safety and immunogenicity of a recombinant tandem-repeat dimeric RBD-based protein subunit vaccine (ZF2001) against COVID-19 in adults: Two randomised, double-blind, placebo-controlled, phase 1 and 2 trials

Abstract

Background: Although several COVID-19 vaccines have been developed so far, they will not be sufficient to meet the global demand. Development of a wider range of vaccines, with different mechanisms of action, could help control the spread of SARS-CoV-2 globally. A protein subunit vaccine was developed against COVID-19 using a dimeric form of the receptor-binding domain (RBD) of the SARS-CoV-2 spike protein as the antigen. It was aimed to assess the safety and immunogenicity of this vaccine, ZF2001, and determine the appropriate dose and schedule for an efficacy study.

Methods: Two randomised, double-blind, placebo-controlled, phase 1 and phase 2 trials was done. Phase 1 was done at two university hospitals in Chongqing and Beijing, China, and phase 2 was done at the Hunan Provincial Center for Disease Control and Prevention in Xiangtan, China. Healthy adults aged 18–59 years, without a history of SARS-CoV or SARS-CoV-2 infection, an RT-PCR-positive test result for SARS-CoV-2, a history of contact with confirmed or suspected COVID-19 cases, and severe allergies to any component of the vaccine were eligible for enrolment. In phase 1, participants were randomly assigned (2:2:1) to receive three doses of the vaccine (25 μg or 50 μg) or placebo intramuscularly, 30 days apart. In phase 2, participants were randomly assigned (1:1:1:1:1:1) to receive the vaccine (25 μg or 50 μg) or placebo intramuscularly, 30 days apart, in either a two-dose schedule or a three-dose schedule. Investigators, participants, and the laboratory team were masked to group allocation. For phase 1, the primary outcome was safety, measured by the occurrence of adverse

events and serious adverse events. For phase 2, the primary outcome was safety and immunogenicity (the seroconversion rate and the magnitude, in geometric mean titres [GMTs], of SARS-CoV-2-neutralising antibodies). Analyses were done on an intention-to-treat and per-protocol basis. These trials are registered with ClinicalTrials.gov (NCT04445194 and NCT04466085) and participant follow-up is ongoing.

Findings: Between June 22 and July 3, 2020, 50 participants were enrolled into the phase 1 trial and randomly assigned to receive three doses of placebo (n=10), the 25 μg vaccine (n=20), or the 50 μg vaccine (n=20). The mean age of participants was 32·6 (SD 9·4) years. Between July 12 and July 17, 2020, 900 participants were enrolled into the phase 2 trial and randomly assigned to receive two doses of placebo (n=150), 25 μg vaccine (n=150), or 50 μg vaccine (n=150), or three doses of placebo (n=150), 25 μg vaccine (n=150), or 50 μg vaccine (n=150). The mean age of participants was 43·5 (SD 9·2) years. In both phase 1 and phase 2, adverse events reported within 30 days after vaccination were mild or moderate (grade 1 or 2) in most cases (phase 1: six [60%] of ten participants in the placebo group, 14 [70%] of 20 in the 25 μg group, and 18 [90%] of 20 in the 50 μg group; phase 2: 37 [25%] of 150 in the two-dose placebo group, 43 [29%] of 150 in the two-dose 25 μg group, 50 [33%] of 150 in the two-dose 50 μg group, 47 [31%] of 150 in the three-dose placebo group, 72 [48%] of 150 in the three-dose 25 μg group, and 65 [43%] of 150 in the three-dose 50 μg group). In phase 1, two (10%) grade 3 or worse adverse events were reported in the 50 μg group. In phase 2, grade 3 or worse adverse events were reported by 18 participants (four [3%] in the two-dose 25 μg vaccine group, two [1%] in the two-dose 50 μg vaccine group, two [1%] in the three-dose placebo group, four [3%] in the three-dose 25 μg vaccine group, and six [4%] in the three-dose 50 μg vaccine group), and 11 were considered vaccine related (two [1%] in the two-dose 25 μg vaccine group, one [1%] in the two-dose 50 μg vaccine group, one [1%] in the three-dose placebo group, two [1%] in the three-dose 25 μg vaccine group, and five [3%] in the three-dose 50 μg vaccine group); seven participants reported serious adverse events (one [1%] in the two-dose 25 μg vaccine group, one [1%] in the two-dose 50 μg vaccine group, two [1%] in the three-dose placebo group, one [1%] in the three-dose 25 μg vaccine group, and two [1%] in the three-dose 50 μg vaccine group), but none was considered vaccine related. In phase 2, on the two-dose schedule, seroconversion rates of neutralising antibodies 14 days after the second dose were 76% (114 of 150 participants) in the 25 μg group and 72% (108 of 150) in the 50

μg group; on the three-dose schedule, seroconversion rates of neutralising antibodies 14 days after the third dose were 97% (143 of 148 participants) in the 25 μg group and 93% (138 of 148) in the 50 μg group. In the two-dose groups in phase 2, the SARS-CoV-2-neutralising GMTs 14 days after the second dose were 17·7 (95% CI 13·6–23·1) in the 25 μg group and 14·1 (10·8–18·3) in the 50 μg group. In the three-dose groups in phase 2, the SARS-CoV-2-neutralising GMTs 14 days after the third dose were 102·5 (95% CI 81·8–128·5) in the 25 μg group and 69·1 (53·0–90·0) in the 50 μg group.

Interpretation: The protein subunit vaccine ZF2001 appears to be well tolerated and immunogenic. The safety and immunogenicity data from the phase 1 and 2 trials support the use of the 25 μg dose in a three-dose schedule in an ongoing phase 3 trial for large-scale evaluation of ZF2001's safety and efficacy.

Reference

https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00127-4/fulltext

The impact of the SARS-COV-2 pandemic on health services utilization in China: Time-series analyses for 2016–2020

Abstract

Background: The aim of this study is to quantify the effects of the SARS-CoV-2 pandemic on health services utilization in China using over four years of routine health information system data.

Methods: A retrospective observational cohort study of health services was conducted utilization from health facilities at all levels in all provinces of mainland China. We analyzed monthly all-cause health facility visits and inpatient volume in health facilities before and during the SARS-CoV-2 outbreak using nationwide routine health information system data from January 2016 to June 2020. Interrupted time series analyses and segmented negative binomial regression were used to examine changes in healthcare utilization attributable to the pandemic. Stratified analyses by facility type and by provincial Human Development Index (HDI) – an area-level measure of socioeconomic status – were conducted to assess potential heterogeneity in effects.

Findings: In the months before the SARS-CoV-2 outbreak, a positive secular trend in patterns of healthcare utilization was observed. After the SARS-CoV-2 outbreak, we

noted statistically significant decreases in all indicators, with all indicators achieving their nadir in February 2020. The magnitude of decline in February ranged from 63% (95% CI 61–65%; p<0•0001) in all-cause visits at hospitals in regions with high HDI and 71% (95% CI 70–72%; p<0•0001) in all-cause visits at primary care clinics to 33% (95% CI 24–42%; p<0•0001) in inpatient volume and 10% (95% CI 3–17%; p = 0•0076) in all-cause visits at township health centers (THC) in regions with low HDI. The reduction in health facility visits was greater than that in the number of outpatients discharged (51% versus 48%; p<0•0079). The reductions in both health facility visits and inpatient volume were greater in hospitals than in primary health care facilities (p<0•0001) and greater in developed regions than in underdeveloped regions (p<0•0001). Following the nadir of health services utilization in February 2020, all indicators showed statistically significant increases. However, even by June 2020, nearly all indicators except outpatient and inpatient volume in regions with low HDI and inpatient volume in private hospitals had not achieved their pre-SARS-COV-2 forecasted levels. In total, we estimated cumulative losses of 1020.5 (95% CI 951.2- 1089.4; P<0.0001) million or 23.9% (95% CI 22.5–25.2%; P<0.0001) health facility visits, and 28.9 (95% CI 26.1–31.6; P<0.0001) million or 21.6% (95% CI 19.7–23.4%; P<0.0001) inpatients as of June 2020.

Interpretation: Inpatient and outpatient health services utilization in China declined significantly after the SARS-CoV-2 outbreak, likely due to changes in patient and provider behaviors, suspension of health facilities or their non-emergency services, massive mobility restrictions, and the potential reduction in the risk of non-SARS-COV-2 diseases. All indicators rebounded beginning in March but most had not recovered to their pre-SARS-COV-2 levels as of June 2020.

Reference

https://www.thelancet.com/journals/lanwpc/article/PIIS2666-6065(21)00031-6/fulltext

The first and second waves of the COVID-19 pandemic in Africa: A cross-sectional study

Abstract

Background: Although the first wave of the COVID-19 pandemic progressed more slowly in Africa than the rest of the world, by December, 2020, the second wave appeared to be much more aggressive with many more cases. To date, the pandemic

situation in all 55 African Union (AU) Member States has not been comprehensively reviewed. It was aimed to evaluate reported COVID-19 epidemiology data to better understand the pandemic's progression in Africa.

Methods: A cross-sectional analysis was done between Feb 14 and Dec 31, 2020, using COVID-19 epidemiological, testing, and mitigation strategy data reported by AU Member States to assess trends and identify the response and mitigation efforts at the country, regional, and continent levels. Descriptive analyses was done on the variables of interest including cumulative and weekly incidence rates, case fatality ratios (CFRs), tests per case ratios, growth rates, and public health and social measures in place.

Findings: As of Dec 31, 2020, African countries had reported 2 763 421 COVID-19 cases and 65 602 deaths, accounting for 3·4% of the 82 312 150 cases and 3·6% of the 1 798 994 deaths reported globally. Nine of the 55 countries accounted for more than 82·6% (2 283 613) of reported cases. 18 countries reported CFRs greater than the global CFR (2·2%). 17 Countries reported test per case ratios less than the recommended ten to 30 tests per case ratio range. At the peak of the first wave in Africa in July, 2020, the mean daily number of new cases was 18 273. As of Dec 31, 2020, 40 (73%) countries had experienced or were experiencing their second wave of cases with the continent reporting a mean of 23 790 daily new cases for epidemiological week 53. 48 (96%) of 50 Member States had five or more stringent public health and social measures in place by April 15, 2020, but this number had decreased to 36 (72%) as of Dec 31, 2020, despite an increase in cases in the preceding month.

Reference

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00632-2/fulltext

Multi-cohort analysis of host immune response identifies conserved protective and detrimental modules associated with severity across viruses

Abstract

Viral infections induce a conserved host response distinct from bacterial infections. It was hypothesized that the conserved response is associated with disease severity and is distinct between patients with different outcomes. To test this, we integrated 4,780 blood transcriptome profiles from patients aged 0 to 90 years infected with one of 16

viruses, including SARS-CoV-2, Ebola, chikungunya, and influenza, across 34 cohorts from 18 countries, and single-cell RNA sequencing profiles of 702,970 immune cells from 289 samples across three cohorts. Severe viral infection was associated with increased hematopoiesis, myelopoiesis, and myeloid-derived suppressor cells. We identified protective and detrimental gene modules that defined distinct trajectories associated with mild versus severe outcomes. The interferon response was decoupled from the protective host response in patients with severe outcomes. These findings were consistent, irrespective of age and virus, and provide insights to accelerate the development of diagnostics and host-directed therapies to improve global pandemic preparedness.

Reference

https://www.cell.com/immunity/fulltext/S1074-7613(21)00114-X

Publication Date: Mar 23, 2021

Pre-existing conditions are associated with COVID-19 patients' hospitalization, despite confirmed clearance of SARS-CoV-2 virus

Abstract

Background: Consecutive negative SARS-CoV-2 PCR test results are being considered to estimate viral clearance in COVID-19 patients. However, there are anecdotal reports of hospitalization from protracted COVID-19 complications despite such confirmed viral clearance, presenting a clinical conundrum.

Method: A retrospective analysis was conducted of 222 hospitalized COVID-19 patients to compare those that were readmitted post-viral clearance (hospitalized post-clearance cohort, n = 49) with those that were not re-admitted post-viral clearance (non-hospitalized post-clearance cohort, n = 173) between February and October 2020. In order to differentiate these two cohorts, we used neural network models for the 'augmented curation' of comorbidities and complications with positive sentiment in the Electronic Hosptial Records physician notes.

Finding: In the year preceding COVID-19 onset, anemia (n = 13 [26.5%], p-value: 0.007), cardiac arrhythmias (n = 14 [28.6%], p-value: 0.015), and acute kidney injury (n

= 7 [14.3%], p-value: 0.030) were significantly enriched in the physician notes of the hospitalized post-clearance cohort.

Interpretation: Overall, this retrospective study highlights specific pre-existing conditions that are associated with higher hospitalization rates in COVID-19 patients despite viral clearance and motivates follow-up prospective research into the associated risk factors.

Reference

https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00073-0/fulltext

A comprehensive analysis and resource to use CRISPR-Cas13 for broad-spectrum targeting of RNA viruses

Abstract

The COVID-19 pandemic caused by SARS-CoV-2 and variants has led to significant mortality. We recently reported that an RNA-targeting CRISPR-Cas13 system, termed prophylactic antiviral CRISPR in human (PAC-MAN), offered an antiviral strategy against SARS-CoV-2 and influenza A virus. Here, we expand in silico analysis to use PAC-MAN to target a broad spectrum of human- or livestock-infectious RNA viruses with high specificity, coverage, and predicted efficiency. The analysis reveals that a minimal set of 14 crRNAs is able to target >90% of human-infectious viruses across 10 RNA virus families. It was predicted that a set of 5 experimentally validated crRNAs can target new SARS-CoV-2 variant sequences with zero mismatches. An online resource was also built to support community use of CRISPR-Cas13 for broad-spectrum RNA virus targeting. The work provides a new bioinformatic resource for using CRISPR-Cas13 to target diverse RNA viruses in order to facilitate development of CRISPR-based antivirals.

Reference

https://www.cell.com/cell-reports-medicine/fulltext/S2666-3791(21)00061-6

Phylogenomic analysis of COVID-19 summer and winter outbreaks in Hong Kong: An observational study

Abstract

Background: Viral genomic surveillance is vital for understanding the transmission of COVID-19. In Hong Kong, breakthrough outbreaks have occurred in July (third wave) and November (fourth wave) 2020. We used whole viral genome analysis to study the characteristics of these waves.

Method: 509 SARS-CoV-2 genomes were analyzed, which were collected from Hong Kong patients between 22nd January and 29th November, 2020. Phylogenetic and phylodynamic analyses were performed, and were interpreted with epidemiological information.

Finding: During the third and fourth waves, diverse SARS-CoV-2 genomes were identified among imported infections. Conversely, local infections were dominated by a single lineage during each wave, with 96.6% (259/268) in the third wave and 100% (73/73) in the fourth wave belonging to B.1.1.63 and B.1.36.27 lineages, respectively. While B.1.1.63 lineage was imported 2 weeks before the beginning of the third wave, B.1.36.27 lineage has circulated in Hong Kong for 2 months prior to the fourth wave. During the fourth wave, 50.7% (37/73) of local infections in November was identical to the viral genome from an imported case in September. Within B.1.1.63 or B.1.36.27 lineage in our cohort, the most common non-synonymous mutations occurred at the helicase (nsp13) gene.

Interpretation: Although stringent measures have prevented most imported cases from spreading in Hong Kong, a single lineage with low-level local transmission in October and early November was responsible for the fourth wave. A superspreading event or lower temperature in November may have facilitated the spread of the B.1.36.27 lineage.

Reference

https://www.thelancet.com/journals/lanwpc/article/PIIS2666-6065(21)00039-0/fulltext

Antivirals with common targets against highly pathogenic viruses

Abstract

Historically, emerging viruses appear constantly and have cost millions of human lives. Currently, climate change and intense globalization have created favorable conditions for viral transmission. Therefore, effective antivirals, especially those targeting the conserved protein in multiple unrelated viruses, such as the compounds targeting RNA-dependent RNA polymerase, are urgently needed to combat more emerging and re-emerging viruses in the future. Here we reviewed the development of antivirals with common targets, including those against the same protein across viruses, or the same viral function, to provide clues for development of antivirals for future epidemics.

Reference

https://www.cell.com/cell/fulltext/S0092-8674(21)00163-X

Novel approaches for vaccine development

Abstract

Vaccines are critical tools for maintaining global health. Traditional vaccine technologies have been used across a wide range of bacterial and viral pathogens, yet there are a number of examples where they have not been successful, such as for persistent infections, rapidly evolving pathogens with high sequence variability, complex viral antigens, and emerging pathogens. Novel technologies such as nucleic acid and viral vector vaccines offer the potential to revolutionize vaccine development as they are well-suited to address existing technology limitations. In this review, we discuss the current state of RNA vaccines, recombinant adenovirus vector-based vaccines, and advances from biomaterials and engineering that address these important public health challenges.

Reference

https://www.cell.com/cell/fulltext/S0092-8674(21)00219-1

Acute psychological impact on COVID-19 patients in Hubei: A multicenter observational study

Abstract

Antibodies with heavy chains that derive from the VH1-2 gene constitute some of the most potent SARS-CoV-2-neutralizing antibodies yet identified. To provide insight into whether these genetic similarities inform common modes of recognition, we determined structures of the SARS-CoV-2 spike in complex with three VH1-2-derived antibodies: 2-15, 2-43, and H4. All three utilize VH1-2-encoded motifs to recognize the receptor-binding domain (RBD), with heavy chain N53I enhancing binding and light chain tyrosines recognizing F486RBD. Despite these similarities, class members bind both RBD-up and -down conformations of the spike, with a subset of antibodies utilizing elongated CDRH3s to recognize glycan N343 on a neighboring RBD – a quaternary interaction accommodated by an increase in RBD separation of up to 12 Å. The VH1-2-antibody class thus utilizes modular recognition encoded by modular genetic elements to effect potent neutralization, with VH-gene component specifying recognition of RBD and CDRH3 component specifying quaternary interactions.

Reference

https://www.cell.com/cell-reports/fulltext/S2211-1247(21)00264-3

PERSPECTIVE

Publication Date: Mar 19, 2021

SARS-CoV-2 transmission without symptoms

Transmission without symptoms critically contributes to the unabated spread of SARS-CoV-2 and presents a considerable infection prevention challenge. Although asymptomatic individuals appear to be contagious for a shorter period of time and may pose a lower transmission risk, they still pose a substantial public health risk as they are more likely to be out in the community. It is unclear how vaccination will affect the number of asymptomatic cases, although preliminary data suggest that mass immunization will reduce infection overall, thus reducing transmission. For presymptomatic cases, research has shown that viral shedding is highest just before and for a few days after symptoms begin, which is a critical time to ensure that individuals who may not realize they have been exposed stay home when possible and practice risk reduction efforts when in the community. Until there is widespread implementation of robust surveillance and epidemiological measures that allow us to put out these smokeless fires, the COVID-19 pandemic cannot be fully extinguished. For more details, read the link given below.

Reference

https://science.sciencemag.org/content/371/6535/1206

REPORT

Publication Date: Mar 23, 2021

Spatial mapping of SARS-CoV-2 and H1N1 lung injury identifies differential transcriptional signatures

Severe SARS-CoV-2 infection often leads to development of acute respiratory distress syndrome (ARDS), with profound pulmonary patho-histological changes post-mortem. It is not clear if ARDS from SARS-CoV-2 is similar to that observed in Influenza H1N1, another common viral cause of lung injury. Here, we analyze specific ARDS regions of interest utilizing a spatial transcriptomic platform on autopsy-derived lung tissue from patients with SARS-CoV-2 (n=3), H1N1 (n=3), and a dual infected individual (n=1). Enhanced gene signatures in alveolar epithelium, vascular tissue, and lung macrophages identify not only increased regional coagulopathy, but also increased extracellular remodeling, alternative macrophage activation, and squamous metaplasia of type II pneumocytes in SARS- CoV-2. Both the H1N1 and dual infected transcriptome demonstrated an enhanced antiviral response compared to SARS-CoV-2. The results uncover regional transcriptional changes related to tissue damage/remodeling, altered cellular phenotype, and vascular injury active in SARS-CoV-2 and presents therapeutic targets for COVID-19 related ARDS.

Reference

https://www.cell.com/cell-reports-medicine/fulltext/S2666-3791(21)00058-6

The impact of population-wide rapid antigen testing on SARS-CoV-2 prevalence in Slovakia

Slovakia conducted multiple rounds of population-wide rapid antigen testing for SARS-CoV-2 in late 2020, combined with a period of additional contact restrictions. Observed prevalence decreased by 58% (95% CI: 57-58%) within one week in the 45 counties that were subject to two rounds of mass testing, an estimate that remained robust when adjusting for multiple potential confounders. Adjusting for epidemic growth of 4.4% (1.1-6.9%) per day preceding the mass testing campaign, the estimated decrease in prevalence compared to a scenario of unmitigated growth was 70% (67-73%).

Modelling indicated that this decrease could not be explained solely by infection control measures, but required the additional impact of isolation and quarantine of household members of those testing positive.

Reference

https://science.sciencemag.org/content/early/2021/03/26/science.abf9648

Publication Date: Mar 22, 2021

Phylogenomic tracing of asymptomatic transmission in a COVID-19 outbreak

SARS-CoV-2 has caused over 100 million deaths and continues to spread rapidly around the world. Asymptomatic transmission of SARS-CoV-2 is the Achilles' heel of COVID-19 public health control measure. Phylogenomic data on SARS-CoV-2 could provide more direct information about asymptomatic transmission. In the present study, using a novel MINERVA sequencing technology, we traced asymptomatic transmission of COVID-19 patients in Beijing, China. 178 close-contacts were quarantined, and 14 COVID-19 patients were laboratory-confirmed by RT-PCR. We provide direct phylogenomic evidence of asymptomatic transmission by constructing the median joining network in the cluster. This data could help us to determine whether the current symptom-based screening should cover asymptomatic persons.

Reference

https://www.cell.com/the-innovation/fulltext/S2666-6758(21)00024-2

Publication Date: Mar 20, 2021

Infection and vaccine-induced antibody binding and neutralization of the B.1.351 SARS-CoV-2 variant

The emergence of SARS-CoV-2 variants with mutations in the spike protein is raising concerns about the efficacy of infection- or vaccine-induced antibodies. It was compared antibody binding and live virus neutralization of sera from naturally infected and Moderna vaccinated individuals against two SARS-CoV-2 variants, B.1 containing the spike mutation D614G and the emerging B.1.351 variant containing additional spike mutations and deletions. Sera from acutely-infected and convalescent COVID-19

patients exhibited a 3-fold reduction in binding antibody titers to the B.1.351 variant receptor binding domain of the spike protein and a 3.5-fold reduction in neutralizing antibody titers against SARS-CoV-2 B.1.351 variant compared to the B.1 variant. Similar results were seen with sera from Moderna vaccinated individuals. Despite reduced antibody titers against the B.1.351 variant, sera from infected and vaccinated individuals containing polyclonal antibodies to the spike protein could still neutralize SARS-CoV-2 B.1.351, suggesting that protective humoral immunity may be retained against this variant.

Reference

https://www.cell.com/cell-host-microbe/fulltext/S1931-3128(21)00137-2

SARS CoV-2 spike variants exhibit differential infectivity and neutralization resistance to convalescent or post-vaccination sera

Towards eradicating the COVID-19 pandemic, vaccines that induce high humoral and cellular immune responses are essential. However, SARS-CoV-2 variants have begun to emerge and raise concern, as they potentially compromise vaccine efficiency. Here neutralization potency of convalescent or Pfizer-BTN162b2 post-vaccination sera against pseudoviruses were monitored, displaying spike proteins derived from wild-type SARS-CoV2, or its UK-B.1.1.7 and SA-B.1.351 variants. Compared to convalescent sera, vaccination induces high titers of neutralizing antibodies, which exhibit efficient neutralization potency against pseudovirus carrying wild-type SARS-CoV2. However, while wild-type and UK-N501Y pseudoviruses were similarly neutralized, those displaying SA-N501Y/K417N/E484K spike mutations moderately resist neutralization. Contribution of single or combined spike mutations to neutralization and infectivity were monitored, highlighting mechanisms by which viral infectivity and neutralization resistance are enhanced by N501Y or E484K/K417N mutations. The study validates the clinical efficacy of the Pfizer vaccine, but raises concerns regarding its efficacy against specific SARS-CoV-2 circulating variants.

Reference

https://www.cell.com/cell-host-microbe/fulltext/S1931-3128(21)00136-0

SARS-CoV-2 variants B.1.351 and P.1 escape from neutralizing antibodies

The global spread of SARS-CoV-2/COVID-19 is devastating health systems and economies worldwide. Recombinant or vaccine-induced neutralizing antibodies are used to combat the COVID-19 pandemic. However, the recently emerged SARS-CoV-2 variants B.1.1.7 (UK), B.1.351 (South Africa) and P.1 (Brazil) harbor mutations in the viral spike (S) protein that may alter virus-host cell interactions and confer resistance to inhibitors and antibodies. Here, using pseudoparticles, we show that entry of all variants into human cells is susceptible to blockade by the entry inhibitors soluble ACE2, Camostat, EK-1 and EK-1-C4. In contrast, entry of the B.1.351 and P.1 variant was partially (Casirivimab) or fully (Bamlanivimab) resistant to antibodies used for COVID-19 treatment. Moreover, entry of these variants was less efficiently inhibited by plasma from convalescent COVID-19 patients and sera from BNT162b2 vaccinated individuals. These results suggest that SARS-CoV-2 may escape neutralizing antibody responses, which has important implications for efforts to contain the pandemic.

Reference

https://www.cell.com/cell/fulltext/S0092-8674(21)00367-6

Publication Date: Mar 18, 2021

Timing the SARS-CoV-2 index case in Hubei province

Understanding when SARS-CoV-2 emerged is critical to evaluating our current approach to monitoring novel zoonotic pathogens and understanding the failure of early containment and mitigation efforts for COVID-19. We employed a coalescent framework to combine retrospective molecular clock inference with forward epidemiological simulations to determine how long SARS-CoV-2 could have circulated prior to the time of the most recent common ancestor. Our results define the period between mid-October and mid-November 2019 as the plausible interval when the first case of SARS-CoV-2 emerged in Hubei province. By characterizing the likely dynamics of the virus before it was discovered, we show that over two-thirds of SARS-CoV-2-like zoonotic events would be self-limited, dying out without igniting a pandemic. Our findings highlight the shortcomings of zoonosis surveillance approaches for detecting highly contagious pathogens with moderate mortality rates.

Reference

https://science.sciencemag.org/content/early/2021/03/17/science.abf8003