Researcher

SARS-CoV-2 Research Literatures

Mark Herbert

World Development Institute
39-06 Main Street, Flushing, Queens, New York 11354, USA, ma708090@gmail.com

Abstract: Coronavirus disease 2019 (COVID-19) is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The virus is mainly spread during close contact and via respiratory droplets that are produced when a person talks, coughs, or sneezes. Respiratory droplets may be produced during breathing, however, current research indicates that the virus is not considered airborne. People may also contract COVID-19 by touching a contaminated surface (Fomite) and then inadvertently transfer the pathogen to a mucous membrane (such as the eyes, nose, or mouth). It is most contagious when people are symptomatic, although spread may be possible before symptoms appear. The virus can live on surfaces up to 72 hours. Time from exposure to onset of symptoms is generally between two and fourteen days, with an average of five days. The standard method of diagnosis is by reverse transcription polymerase chain reaction (rRT-PCR) from a nasopharyngeal swab. The infection can also be diagnosed from a combination of symptoms, risk factors and a chest CT scan showing features of pneumonia. This article introduces recent research reports as references in the related studies.

Key words: SARS-CoV-2; life; research; literature

Introduction

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The virus is mainly spread during close contact and via respiratory droplets that are produced when a person talks, coughs, or sneezes. Respiratory droplets may be produced during breathing, however, current research indicates that the virus is not considered airborne. People may also contract COVID-19 by touching a contaminated surface (Fomite) and then inadvertently transfer the pathogen to a mucous membrane (such as the eyes, nose, or mouth). It is most contagious when people are symptomatic, although spread may be possible before symptoms appear. The virus can live on surfaces up to 72 hours. Time from exposure to onset of symptoms is generally between two and fourteen days, with an average of five days. The standard method of diagnosis is by reverse transcription polymerase chain reaction (rRT-PCR) from a nasopharyngeal swab. The infection can also be diagnosed from a combination of symptoms, risk factors and a chest CT scan showing features of pneumonia. This article introduces recent research reports as references in the related studies.

The following introduces recent reports as references in the related studies.

Ahmed, S. F., et al. (2020). "Preliminary Identification of Potential Vaccine Targets for the COVID-19 Coronavirus (SARS-CoV-2) Based on SARS-CoV Immunological Studies." Viruses **12**(3).

The beginning of 2020 has seen the emergence of COVID-19 outbreak caused by a novel coronavirus, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). There is an imminent need to better understand this new virus and to develop ways to control its spread. In this study, we sought to gain insights for vaccine design against SARS-CoV-2 by considering the high genetic similarity between SARS-CoV-2 and SARS-CoV, which caused the outbreak in 2003, and leveraging existing immunological studies of SARS-CoV. By screening the experimentally-determined SARS-CoV-derived B cell and T cell epitopes in the immunogenic structural proteins of SARS-CoV, we identified a set of B cell and T cell epitopes derived from the spike (S) and nucleocapsid (N) proteins that map identically to SARS-CoV-2 proteins. As no mutation has been observed in these identified epitopes among the 120 available SARS-CoV-2 sequences (as of 21 February 2020), immune targeting of these epitopes may potentially offer protection against this novel virus. For the T cell epitopes, we performed a population coverage analysis of the associated MHC alleles and proposed a set of epitopes that is estimated to provide broad coverage globally, as well as in China. Our findings provide a

screened set of epitopes that can help guide experimental efforts towards the development of vaccines against SARS-CoV-2.

Ashour, H. M., et al. (2020). "Insights into the Recent 2019 Novel Coronavirus (SARS-CoV-2) in Light of Past Human Coronavirus Outbreaks." Pathogens **9**(3).

Coronaviruses (CoVs) are RNA viruses that have become a major public health concern since the Severe Acute Respiratory Syndrome-CoV (SARS-CoV) outbreak in 2002. The continuous evolution of coronaviruses was further highlighted with the emergence of the Middle East Respiratory Syndrome-CoV (MERS-CoV) outbreak in 2012. Currently, the world is concerned about the 2019 novel CoV (SARS-CoV-2) that was initially identified in the city of Wuhan, China in December 2019. Patients presented with severe viral pneumonia and respiratory illness. The number of cases has been mounting since then. As of late February 2020, tens of thousands of cases and several thousand deaths have been reported in China alone, in addition to thousands of cases in other countries. Although the fatality rate of SARS-CoV-2 is currently lower than SARS-CoV, the virus seems to be highly contagious based on the number of infected cases to date. In this review, we discuss structure, genome organization, entry of CoVs into target cells, and provide insights into past and present outbreaks. The future of human CoV outbreaks will not only depend on how the viruses will evolve, but will also depend on how we develop efficient prevention and treatment strategies to deal with this continuous threat.

Baglivo, M., et al. (2020). "Natural small molecules as inhibitors of coronavirus lipid-dependent attachment to host cells: a possible strategy for reducing SARS-COV-2 infectivity?" Acta Biomed **91**(1): 161-164.

BACKGROUND: Viral infectivity depends on interactions between components of the host cell plasma membrane and the virus envelope. Here we review strategies that could help stem the advance of the SARS-COV-2 epidemic. METHODS AND RESULTS: We focus on the role of lipid structures, such as lipid rafts and cholesterol, involved in the process, mediated by endocytosis, by which viruses attach to and infect cells. Previous studies have shown that many naturally derived substances, such as cyclodextrin and sterols, could reduce the infectivity of many types of viruses, including the coronavirus family, through interference with lipid-dependent attachment to human host cells. CONCLUSIONS: Certain molecules prove able to reduce the infectivity of some coronaviruses, possibly by inhibiting viral lipid-dependent attachment to host cells. More

research into these molecules and methods would be worthwhile as it could provide insights the mechanism of transmission of SARS-COV-2 and, into how they could become a basis for new antiviral strategies.

Basile, C., et al. (2020). "Recommendations for the prevention, mitigation and containment of the emerging SARS-CoV-2 (COVID-19) pandemic in haemodialysis centres." Nephrol Dial Transplant.

COVID-19, a disease caused by a novel coronavirus, is a major global human threat that has turned into a pandemic. This novel coronavirus has specifically high morbidity in the elderly and in comorbid populations. Uraemic patients on dialysis combine an intrinsic fragility and a very frequent burden of comorbidities with a specific setting in which many patients are repeatedly treated in the same area (haemodialysis centres). Moreover, if infected, the intensity of dialysis requiring specialized resources and staff is further complicated by requirements for isolation, control and prevention, putting healthcare systems under exceptional additional strain. Therefore, all measures to slow if not to eradicate the pandemic and to control unmanageably high incidence rates must be taken very seriously. The aim of the present review of the European Dialysis (EUDIAL) Working Group of ERA-EDTA is to provide recommendations for the prevention, mitigation and containment in haemodialysis centres of the emerging COVID-19 pandemic. The management of patients on dialysis affected by COVID-19 must be carried out according to strict protocols to minimize the risk for other patients and personnel taking care of these patients. Measures of prevention, protection, screening, isolation and distribution have been shown to be efficient in similar settings. They are essential in the management of the pandemic and should be taken in the early stages of the disease.

Bhattacharya, M., et al. (2020). "Development of epitope-based peptide vaccine against novel coronavirus 2019 (SARS-COV-2): Immunoinformatics approach." J Med Virol.

Recently, a novel coronavirus (SARS-COV-2) emerged which is responsible for the recent outbreak in Wuhan, China. Genetically, it is closely related to SARS-CoV and MERS-CoV. The situation is getting worse and worse, therefore, there is an urgent need for designing a suitable peptide vaccine component against the SARS-COV-2. Here, we characterized spike glycoprotein to obtain immunogenic epitopes. Next, we chose 13 Major Histocompatibility Complex-(MHC) I and 3 MHC-II epitopes, having antigenic properties. These epitopes are usually linked to specific linkers to build vaccine components and molecularly dock on toll-like receptor-5 to get binding

affinity. Therefore, to provide a fast immunogenic profile of these epitopes, we performed immunoinformatics analysis so that the rapid development of the vaccine might bring this disastrous situation to the end earlier.

Bordi, L., et al. (2020). "Differential diagnosis of illness in patients under investigation for the novel coronavirus (SARS-CoV-2), Italy, February 2020." Euro Surveill **25**(8).

A novel coronavirus (SARS-CoV-2) has been identified as the causative pathogen of an ongoing outbreak of respiratory disease, now named COVID-19. Most cases and sustained transmission occurred in China, but travel-associated cases have been reported in other countries, including Europe and Italy. Since the symptoms are similar to other respiratory infections, differential diagnosis in travellers arriving from countries with wide-spread COVID-19 must include other more common infections such as influenza and other respiratory tract diseases.

Bryson-Cahn, C., et al. (2020). "A Novel Approach for a Novel Pathogen: using a home assessment team to evaluate patients for 2019 novel coronavirus (SARS-CoV-2)." Clin Infect Dis.

Thousands of people in the United States have required testing for SARS-CoV-2. Evaluation for a special pathogen is resource intensive. We report an innovative approach to home assessment that, in collaboration with public health, enables safe evaluation and specimen collection outside the healthcare setting, avoiding unnecessary exposures and resource utilization.

Cardenas-Conejo, Y., et al. (2020). "An exclusive 42 amino acid signature in pp1ab protein provides insights into the evolutive history of the 2019 novel human-pathogenic coronavirus (SARS-CoV-2)." J Med Virol.

The city of Wuhan, Hubei province, China, was the origin of a severe pneumonia outbreak in December 2019, attributed to a novel coronavirus (severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]), causing a total of 2761 deaths and 81109 cases (25 February 2020). SARS-CoV-2 belongs to genus Betacoronavirus, subgenus Sarbecovirus. The polyprotein 1ab (pp1ab) remains unstudied thoroughly since it is similar to other sarbecoviruses. In this short communication, we performed phylogenetic-structural sequence analysis of pp1ab protein of SARS-CoV-2. The analysis showed that the viral pp1ab has not changed in most isolates throughout the outbreak time, but interestingly a deletion of 8 aa in the virulence factor nonstructural protein 1 was found in a virus isolated from a Japanese

patient that did not display critical symptoms. While comparing pp1ab protein with other betacoronaviruses, we found a 42 amino acid signature that is only present in SARS-CoV-2 (AS-SCoV2). Members from clade 2 of sarbecoviruses have traces of this signature. The AS-SCoV2 located in the acidic-domain of papain-like protein of SARS-CoV-2 and bat-SL-CoV-RatG13 guided us to suggest that the novel 2019 coronavirus probably emerged by genetic drift from bat-SL-CoV-RaTG13. The implication of this amino acid signature in papain-like protein structure arrangement and function is something worth to be explored.

Chen, D., et al. (2020). "Recurrence of positive SARS-CoV-2 RNA in COVID-19: A case report." Int J Infect Dis.

The ongoing outbreak of COVID-19 that began in Wuhan, China, has constituted a Public Health Emergency of International Concern, with cases confirmed in multiple countries. Currently patients are the main source of infection. We report a confirmed case of COVID-19 whose oropharyngeal swab test of SARS-CoV-2 RNA turned positive in convalescence. This case highlights the importance of dynamic surveillance of SARS-CoV-2 RNA for infectivity assessment.

Chen, Y. W., et al. (2020). "Prediction of the SARS-CoV-2 (2019-nCoV) 3C-like protease (3CL (pro)) structure: virtual screening reveals velpatasvir, ledipasvir, and other drug repurposing candidates." F1000Res **9**: 129.

We prepared the three-dimensional model of the SARS-CoV-2 (aka 2019-nCoV) 3C-like protease (3CL (pro)) using the crystal structure of the highly similar (96% identity) ortholog from the SARS-CoV. All residues involved in the catalysis, substrate binding and dimerisation are 100% conserved. Comparison of the polyprotein PP1AB sequences showed 86% identity. The 3C-like cleavage sites on the coronaviral polyproteins are highly conserved. Based on the near-identical substrate specificities and high sequence identities, we are of the opinion that some of the previous progress of specific inhibitors development for the SARS-CoV enzyme can be conferred on its SARS-CoV-2 counterpart. With the 3CL (pro) molecular model, we performed virtual screening for purchasable drugs and proposed 16 candidates for consideration. Among these, the antivirals ledipasvir or velpatasvir are particularly attractive as therapeutics to combat the new coronavirus with minimal side effects, commonly fatigue and headache. The drugs Epclusa (velpatasvir/sofosbuvir) and Harvoni (ledipasvir/sofosbuvir) could be very effective owing to their dual inhibitory actions on two viral enzymes.

Chen, Z., et al. (2020). "[Emergency plan for inter-hospital transfer of newborns with SARS-CoV-2 infection]." Zhongguo Dang Dai Er Ke Za Zhi **22**(3): 226-230.

Since December 2019, the outbreak of coronavirus disease (COVID-19) has become the most serious public health issue. As the special population with immature immune function, newborns with COVID-19 have been reported. Newborns with suspected or confirmed COVID-19 should be transferred to designated hospitals for isolation treatment. An emergency transfer response plan for newborns with COVID-19 has been worked out. This plan puts forward the indications for neonatal COVID-19 transfer, organization management, protection strategies for medical staff, work procedures, and disinfection methods for transfer equipment, in order to provide guidance and suggestions for the inter-hospital transfer of suspected or confirmed neonatal COVID-19.

Cheng, V. C. C., et al. (2020). "Escalating infection control response to the rapidly evolving epidemiology of the Coronavirus disease 2019 (COVID-19) due to SARS-CoV-2 in Hong Kong." Infect Control Hosp Epidemiol: 1-24.

BACKGROUND: To describe the infection control preparedness for Coronavirus Disease (COVID-19) due to SARS-CoV-2 [previously known as 2019-novel coronavirus] in the first 42 days after announcement of a cluster of pneumonia in China, on 31 December 2019 (day 1) in Hong Kong. METHODS: A bundle approach of active and enhanced laboratory surveillance, early airborne infection isolation, rapid molecular diagnostic testing, and contact tracing for healthcare workers (HCWs) with unprotected exposure in the hospitals was implemented. Epidemiological characteristics of confirmed cases, environmental and air samples were collected and analyzed. RESULTS: From day 1 to day 42, forty-two (3.3%) of 1275 patients fulfilling active (n=29) and enhanced laboratory surveillance (n=13) confirmed to have SARS-CoV-2 infection. The number of locally acquired case significantly increased from 1 (7.7%) of 13 [day 22 to day 32] to 27 (93.1%) of 29 confirmed case [day 33 to day 42] (p<0.001). Twenty-eight patients (66.6%) came from 8 family clusters. Eleven (2.7%) of 413 HCWs caring these confirmed cases were found to have unprotected exposure requiring quarantine for 14 days. None of them was infected and nosocomial transmission of SARS-CoV-2 was not observed. Environmental surveillance performed in a patient with viral load of 3.3x106 copies/ml (pooled nasopharyngeal/ throat swab) and 5.9x106 copies/ml (saliva) respectively. SARS-CoV-2 revealed in 1 (7.7%) of 13 environmental samples, but not in 8 air samples collected at a distance of 10 cm from patient's chin with or without wearing a surgical mask. CONCLUSION: Appropriate hospital infection control measures could prevent nosocomial transmission of SARS-CoV-2.

Conti, P., et al. (2020). "Induction of pro-inflammatory cytokines (IL-1 and IL-6) and lung inflammation by Coronavirus-19 (COVI-19 or SARS-CoV-2): anti-inflammatory strategies." J Biol Regul Homeost Agents **34**(2).

Coronavirus-19 (COVI-19) involves humans as well as animals and may cause serious damage to the respiratory tract, including the lung: coronavirus disease (COVID-19). This pathogenic virus has been identified in swabs performed on the throat and nose of patients who suffer from or are suspected of the disease. When COVI-19 infect the upper and lower respiratory tract it can cause mild or highly acute respiratory syndrome with consequent release of pro-inflammatory cytokines, including interleukin (IL)-1beta and IL-6. The binding of COVI-19 to the Toll Like Receptor (TLR) causes the release of pro-IL-1beta which is cleaved by caspase-1, followed by inflammasome activation and production of active mature IL-1beta which is a mediator of lung inflammation, fever and fibrosis. Suppression of pro-inflammatory IL-1 family members and IL-6 have been shown to have a therapeutic effect in many inflammatory diseases, including viral infections. Cytokine IL-37 has the ability to suppress innate and acquired immune response and also has the capacity to inhibit inflammation by acting on IL-18Ralpha receptor. IL-37 performs its immunosuppressive activity by acting on mTOR and increasing the adenosine monophosphate (AMP) kinase. This cytokine inhibits class II histocompatibility complex (MHC) molecules and inflammation in inflammatory diseases by suppressing MyD88 and subsequently IL-1beta, IL-6, TNF and CCL2. The suppression of IL-1beta by IL-37 in inflammatory state induced by coronavirus-19 can have a new therapeutic effect previously unknown. Another inhibitory cytokine is IL-38, the newest cytokine of the IL-1 family members, produced by several immune cells including B cells and macrophages. IL-38 is also a suppressor cytokine which inhibits IL-1beta and other pro-inflammatory IL-family members. IL-38 is a potential therapeutic cytokine which inhibits inflammation in viral infections including that caused by coronavirus-19, providing a new relevant strategy.

El Zowalaty, M. E. and J. D. Jarhult (2020). "From SARS to COVID-19: A previously unknown

SARS- related coronavirus (SARS-CoV-2) of pandemic potential infecting humans - Call for a One Health approach." One Health **9**: 100124.

Human coronaviruses continue to pose a threat to human health. The emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in December 2019 which causes coronavirus disease-2019 (COVID-19), an acute respiratory disease marked the third introduction of a highly pathogenic coronavirus into the human population in the twenty-first century. This recent emergence of a previously unknown coronavirus in China leads to huge impacts on humans globally. Covid-19 is a challenge to global public health. Here, we discuss the COVID-19 outbreak in a one health context, highlighting the need for the implementation of one health measures and practices to improve human health and reduce the emergence of pandemic viruses.

Fan, C., et al. (2020). "Perinatal Transmission of COVID-19 Associated SARS-CoV-2: Should We Worry?" Clin Infect Dis.

We presented two cases of COVID-19 associated SARS-CoV-2 infection during third trimester of pregnancy. Both mothers and newborns had excellent outcomes. We failed to identify SARS-CoV-2 in all the products of conception and the newborns. This report provided evidence of low risk of intrauterine infection by vertical transmission of SARS-CoV-2.

Fu, Y., et al. (2020). "Understanding SARS-CoV-2-Mediated Inflammatory Responses: From Mechanisms to Potential Therapeutic Tools." Virol Sin.

Currently there is no effective antiviral therapy for SARS-CoV-2 infection, which frequently leads to fatal inflammatory responses and acute lung injury. Here, we discuss the various mechanisms of SARS-CoV-mediated inflammation. We also assume that SARS-CoV-2 likely shares similar inflammatory responses. Potential therapeutic tools to reduce SARS-CoV-2-induced inflammatory responses include various methods to block FcR activation. In the absence of a proven clinical FcR blocker, the use of intravenous immunoglobulin to block FcR activation may be a viable option for the urgent treatment of pulmonary inflammation to prevent severe lung injury. Such treatment may also be combined with systemic anti-inflammatory drugs or corticosteroids. However, these strategies, as proposed here, remain to be clinically tested for effectiveness.

Ghinai, I., et al. (2020). "First known person-to-person transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in the USA." Lancet.

BACKGROUND: Coronavirus disease 2019 (COVID-19) is a disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), first detected in China in December, 2019. In January, 2020, state, local, and federal public health agencies investigated the first case of COVID-19 in Illinois, USA. METHODS: Patients with confirmed COVID-19 were defined as those with a positive SARS-CoV-2 test. Contacts were people with exposure to a patient with COVID-19 on or after the patient's symptom onset date. Contacts underwent active symptom monitoring for 14 days following their last exposure. Contacts who developed fever, cough, or shortness of breath became persons under investigation and were tested for SARS-CoV-2. A convenience sample of 32 asymptomatic health-care personnel contacts were also tested. FINDINGS: Patient 1-a woman in her 60s-returned from China in mid-January, 2020. One week later, she was hospitalised with pneumonia and tested positive for SARS-CoV-2. Her husband (Patient 2) did not travel but had frequent close contact with his wife. He was admitted 8 days later and tested positive for SARS-CoV-2. Overall, 372 contacts of both cases were identified; 347 underwent active symptom monitoring, including 152 community contacts and 195 health-care personnel. Of monitored contacts, 43 became persons under investigation, in addition to Patient 2. These 43 persons under investigation and all 32 asymptomatic health-care personnel tested negative for SARS-CoV-2. INTERPRETATION: Person-to-person transmission of SARS-CoV-2 occurred between two people with prolonged, unprotected exposure while Patient 1 was symptomatic. Despite active symptom monitoring and testing of symptomatic and some asymptomatic contacts, no further transmission was detected. FUNDING: None.

Giovanetti, M., et al. (2020). "A doubt of multiple introduction of SARS-CoV-2 in Italy: a preliminary overview." J Med Virol.

The emergence of the novel beta Coronavirus, recently renamed as severe acute respiratory syndrome coronavirus 2, SARS-CoV-2, has raised serious concerns due to the virus rapid dissemination worldwide. Nevertheless, there is limited information about the genomic epidemiology of SARS-CoV-2 circulating in Italy from surveillance studies. The shortage of complete genomic sequences available impairs our understanding of the SARS-CoV-2 introduction and establishment in the country. To better understand its dynamics in Italy, we analysed complete genomes of SARS-CoV-2 isolates, obtained directly from clinical samples. Our phylogenetic reconstructions suggest possible multiple introduction of SARS-CoV-2. Continued genomic surveillance strategies are needed to improve monitoring and

understanding of the currently SARS-CoV-2 epidemics, which might help to attenuate public health impact of infectious diseases.

Giwa, A. L., et al. (2020). "Novel 2019 coronavirus SARS-CoV-2 (COVID-19): An updated overview for emergency clinicians." Emerg Med Pract **22**(5): 1-28.

The novel coronavirus, COVID-19, has quickly become a worldwide threat to health, travel, and commerce. This overview analyzes the best information from the early research, including epidemiologic and demographic features from SARS-CoV-1 and MERS-CoV viruses; lessons learned from the experience of an emergency physician in Northern Italy, where the outbreak has devastated the healthcare system; evidence on transmission and prevention through safe use of PPE; evidence and advice on SARS-CoV-2 testing and co-infection; management options; airway management options; steps for rapid sequence intubation in the ED and managing disaster ventilation; and information on managing pediatric and pregnant patients.

Grifoni, A., et al. (2020). "A Sequence Homology and Bioinformatic Approach Can Predict Candidate Targets for Immune Responses to SARS-CoV-2." Cell Host Microbe.

Effective countermeasures against the recent emergence and rapid expansion of the 2019 novel coronavirus (SARS-CoV-2) require the development of data and tools to understand and monitor its spread and immune responses to it. However, little information is available about the targets of immune responses to SARS-CoV-2. We used the Immune Epitope Database and Analysis Resource (IEDB) to catalog available data related to other coronaviruses. This includes SARS-CoV, which has high sequence similarity to SARS-CoV-2 and is the best-characterized coronavirus in terms of epitope responses. We identified multiple specific regions in SARS-CoV-2 that have high homology to the SARS-CoV virus. Parallel bioinformatic predictions identified a priori potential B and T cell epitopes for SARS-CoV-2. The independent identification of the same regions using two approaches reflects the high probability that these regions are promising targets for immune recognition of SARS-CoV-2. These predictions can facilitate effective vaccine design against this virus of high priority.

Gurwitz, D. (2020). "Angiotensin receptor blockers as tentative SARS-CoV-2 therapeutics." Drug Dev Res.

At the time of writing this commentary (February 2020), the coronavirus COVID-19 epidemic has already resulted in more fatalities compared with the SARS and MERS coronavirus epidemics combined. Therapeutics that may assist to contain its rapid spread and reduce its high mortality rates are urgently needed. Developing vaccines against the SARS-CoV-2 virus may take many months. Moreover, vaccines based on viral-encoded peptides may not be effective against future coronavirus epidemics, as virus mutations could make them futile. Indeed, new Influenza virus strains emerge every year, requiring new immunizations. A tentative suggestion based on existing therapeutics, which would likely be resistant to new coronavirus mutations, is to use available angiotensin receptor 1 (AT1R) blockers, such as losartan, as therapeutics for reducing the aggressiveness and mortality from SARS-CoV-2 virus infections. This idea is based on observations that the angiotensin-converting enzyme 2 (ACE2) very likely serves as the binding site for SARS-CoV-2, the strain implicated in the current COVID-19 epidemic, similarly to strain SARS-CoV implicated in the 2002-2003 SARS epidemic. This commentary elaborates on the idea of considering AT1R blockers as tentative treatment for SARS-CoV-2 infections, and proposes a research direction based on datamining of clinical patient records for assessing its feasibility.

Han, H., et al. (2020). "Prominent changes in blood coagulation of patients with SARS-CoV-2 infection." Clin Chem Lab Med.

Background As the number of patients increases, there is a growing understanding of the form of pneumonia sustained by the 2019 novel coronavirus (SARS-CoV-2), which has caused an outbreak in China. Up to now, clinical features and treatment of patients infected with SARS-CoV-2 have been reported in detail. However, the relationship between SARS-CoV-2 and coagulation has been scarcely addressed. Our aim is to investigate the blood coagulation function of patients with SARS-CoV-2 infection. Methods In our study, 94 patients with confirmed SARS-CoV-2 infection were admitted in Renmin Hospital of Wuhan University. We prospectively collect blood coagulation data in these patients and in 40 healthy controls during the same period. Results Antithrombin values in patients were lower than that in the control group (p < 0.001). The values of D-dimer, fibrin/fibrinogen degradation products (FDP), and fibrinogen (FIB) in all SARS-CoV-2 cases were substantially higher than those in healthy controls. Moreover, D-dimer and FDP values in patients with severe SARS-CoV-2 infection were higher than those in patients with milder forms. Compared with healthy controls, prothrombin time

activity (PT-act) was lower in SARS-CoV-2 patients. Thrombin time in critical SARS-CoV-2 patients was also shorter than that in controls. Conclusions The coagulation function in patients with SARS-CoV-2 is significantly deranged compared with healthy people, but monitoring D-dimer and FDP values may be helpful for the early identification of severe cases.

Hill, D. K. J., et al. (2020). "The index case of SARS-CoV-2 in Scotland: a case report." J Infect.

Since its identification in December 2019, SARS-CoV-2 has infected 125,048 persons globally with cases identified in 118 countries across all continents (1). We report on the Scottish index case of SARS-CoV-2 infection, the virus causing COVID-19.

Hoffmann, M., et al. (2020). "SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor." Cell.

The recent emergence of the novel, pathogenic SARS-coronavirus 2 (SARS-CoV-2) in China and its rapid national and international spread pose a global health emergency. Cell entry of coronaviruses depends on binding of the viral spike (S) proteins to cellular receptors and on S protein priming by host cell proteases. Unravelling which cellular factors are used by SARS-CoV-2 for entry might provide insights into viral transmission and reveal therapeutic targets. Here, we demonstrate that SARS-CoV-2 uses the SARS-CoV receptor ACE2 for entry and the serine protease TMPRSS2 for S protein priming. A TMPRSS2 inhibitor approved for clinical use blocked entry and might constitute a treatment option. Finally, we show that the sera from convalescent SARS patients cross-neutralized SARS-2-S-driven entry. Our results reveal important commonalities between SARS-CoV-2 and SARS-CoV infection and identify a potential target for antiviral intervention.

Jiang, X., et al. (2020). "Does SARS-CoV-2 has a longer incubation period than SARS and MERS?" J Med Virol **92**(5): 476-478.

The outbreak of a novel coronavirus (SARS-CoV-2) since December 2019 in Wuhan, the major transportation hub in central China, became an emergency of major international concern. While several etiological studies have begun to reveal the specific biological features of this virus, the epidemic characteristics need to be elucidated. Notably, a long incubation time was reported to be associated with SARS-CoV-2 infection, leading to adjustments in screening and control policies. To avoid the risk of virus spread, all potentially exposed subjects are required to be isolated for 14 days, which is the longest predicted incubation time. However, based on our analysis of a larger dataset available so far, we find there is no observable difference between the incubation time for SARS-CoV-2, severe acute respiratory syndrome coronavirus (SARS-CoV), and middle east respiratory syndrome coronavirus (MERS-CoV), highlighting the need for larger and well-annotated datasets.

Kamel Boulos, M. N. and E. M. Geraghty (2020). "Geographical tracking and mapping of coronavirus disease COVID-19/severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) epidemic and associated events around the world: how 21st century GIS technologies are supporting the global fight against outbreaks and epidemics." Int J Health Geogr **19**(1): 8.

In December 2019, a new virus (initially called 'Novel Coronavirus 2019-nCoV' and later renamed to SARS-CoV-2) causing severe acute respiratory syndrome (coronavirus disease COVID-19) emerged in Wuhan, Hubei Province, China, and rapidly spread to other parts of China and other countries around the world, despite China's massive efforts to contain the disease within Hubei. As with the original SARS-CoV epidemic of 2002/2003 and with seasonal influenza, geographic information systems and methods, including, among other application possibilities, online real-or near-real-time mapping of disease cases and of social media reactions to disease spread, predictive risk mapping using population travel data, and tracing and mapping super-spreader trajectories and contacts across space and time, are proving indispensable for timely and effective epidemic monitoring and response. This paper offers pointers to, and describes, a range of practical online/mobile GIS and mapping dashboards and applications for tracking the 2019/2020 coronavirus epidemic and associated events as they unfold around the world. Some of these dashboards and applications are receiving data updates in near-real-time (at the time of writing), and one of them is meant for individual users (in China) to check if the app user has had any close contact with a person confirmed or suspected to have been infected with SARS-CoV-2 in the recent past. We also discuss additional ways GIS can support the fight against infectious disease outbreaks and epidemics.

Kandeel, M., et al. (2020). "From SARS and MERS CoVs to SARS-CoV-2: Moving toward more biased codon usage in viral structural and nonstructural genes." J Med Virol.

BACKGROUND: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is an emerging disease with fatal outcomes. In this study, a fundamental knowledge gap question is to be resolved by evaluating the differences in biological and pathogenic aspects of SARS-CoV-2 and the changes in

SARS-CoV-2 in comparison with the two prior major COV epidemics, SARS and Middle East respiratory syndrome (MERS) coronaviruses. METHODS: The genome composition, nucleotide analysis, codon usage indices, relative synonymous codons usage, and effective number of codons (ENc) were analyzed in the four structural genes; Spike (S), Envelope (E), membrane (M), and Nucleocapsid (N) genes, and two of the most important nonstructural genes comprising RNA-dependent RNA polymerase and main protease (Mpro) of SARS-CoV-2, Beta-CoV from pangolins, bat SARS, MERS, and SARS CoVs. RESULTS: SARS-CoV-2 prefers pyrimidine rich codons to purines. Most high-frequency codons were ending with A or T, while the low frequency and rare codons were ending with G or C. SARS-CoV-2 structural proteins showed 5 to 20 lower ENc values, compared with SARS, bat SARS, and MERS CoVs. This implies higher codon bias and higher gene expression efficiency of SARS-CoV-2 structural proteins. SARS-CoV-2 encoded the highest number of over-biased and negatively biased codons. Pangolin Beta-CoV showed little differences with SARS-CoV-2 ENc values, compared with SARS, bat SARS, and MERS CoV. CONCLUSION: Extreme bias and lower ENc values of SARS-CoV-2, especially in Spike, Envelope, and Mpro genes, are suggestive for higher gene expression efficiency, compared with SARS, bat SARS, and MERS CoVs.

Khan, S., et al. (2020). "The emergence of a novel coronavirus (SARS-CoV-2), their biology and therapeutic options." J Clin Microbiol.

The new decade of the 21(st) century (2020) started with the emergence of novel coronavirus known as SARS-CoV-2 that caused an epidemic of coronavirus disease (COVID-19) in Wuhan, China. It is the third highly pathogenic and transmissible coronavirus after severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) emerged in humans. The source of origin, transmission to humans and mechanisms associated with the pathogenicity of SARS-CoV-2 are not clear yet, however, its resemblance with SARS-CoV and several other bat coronaviruses was recently confirmed through genome sequencing related studies. The development of therapeutic strategies is necessary in order to prevent further epidemics and cure infected people. In this Review, we summarize current information about the emergence, origin, diversity, and epidemiology of three pathogenic coronaviruses with a specific focus on the current outbreak in Wuhan, China. Furthermore, we discuss the clinical features and potential therapeutic options that may be effective against SARS-CoV-2.

Kim, J. Y., et al. (2020). "Viral Load Kinetics of SARS-CoV-2 Infection in First Two Patients in Korea." J Korean Med Sci 35(7): e86.

As of February 2020, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) outbreak started in China in December 2019 has been spreading in many countries in the world. With the numbers of confirmed cases are increasing, information on the epidemiologic investigation and clinical manifestation have been accumulated. However, data on viral load kinetics in confirmed cases are lacking. Here, we present the viral load kinetics of the first two confirmed patients with mild to moderate illnesses in Korea in whom distinct viral load kinetics are shown. This report suggests that viral load kinetics of SARS-CoV-2 may be different from that of previously reported other coronavirus infections such as SARS-CoV.

Konrad, R., et al. (2020). "Rapid establishment of laboratory diagnostics for the novel coronavirus SARS-CoV-2 in Bavaria, Germany, February 2020." Euro Surveill 25(9).

The need for timely establishment of diagnostic assays arose when Germany was confronted with the first travel-associated outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in Europe. We describe our laboratory experiences during a large contact tracing investigation, comparing previously published real-time RT-PCR assays in different PCR systems and a commercial kit. We found that assay performance using the same primers and probes with different PCR systems varied and the commercial kit performed well.

Lai, A., et al. (2020). "Early phylogenetic estimate of the effective reproduction number of SARS-CoV-2." J Med Virol.

To reconstruct the evolutionary dynamics of the 2019 novel-coronavirus recently causing an outbreak in Wuhan, China, 52 SARS-CoV-2 genomes available on 4 February 2020 at Global Initiative on Sharing All Influenza Data were analyzed. The two models used to estimate the reproduction number (coalescent-based exponential growth and a birth-death skyline method) indicated an estimated mean evolutionary rate of 7.8 x 10(-4) subs/site/year (range, 1.1 x 10(-4) -15 x 10(-4)) and a mean tMRCA of the tree root of 73 days. The estimated R value was 2.6 (range, 2.1-5.1), and increased from 0.8 to 2.4 in December 2019. The estimated mean doubling time of the epidemic was between 3.6 and 4.1 days. This study proves the usefulness of phylogeny in supporting the surveillance of emerging new infections even as the epidemic is growing.

Lai, C. C., et al. (2020). "Asymptomatic carrier state, acute respiratory disease, and pneumonia due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2): Facts and myths." J Microbiol Immunol Infect.

Since the emergence of coronavirus disease 2019 (COVID-19) (formerly known as the 2019 novel coronavirus [2019-nCoV]) in Wuhan, China in December 2019, which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), more than 75,000 cases have been reported in 32 countries/regions, resulting in more than 2000 deaths worldwide. Despite the fact that most COVID-19 cases and mortalities were reported in China, the WHO has declared this outbreak as the sixth public health emergency of international concern. The COVID-19 can present as an asymptomatic carrier state, acute respiratory disease, and pneumonia. Adults represent the population with the highest infection rate; however, neonates, children, and elderly patients can also be infected by SARS-CoV-2. In addition, nosocomial infection of hospitalized patients and healthcare workers, and viral transmission from asymptomatic carriers are possible. The most common finding on chest imaging among patients with pneumonia was ground-glass opacity with bilateral involvement. Severe cases are more likely to be older patients with underlying comorbidities compared to mild cases. Indeed, age and disease severity may be correlated with the outcomes of COVID-19. To date, effective treatment is lacking; however, clinical trials investigating the efficacy of several agents, including remdesivir and chloroquine, are underway in China. Currently, effective infection control intervention is the only way to prevent the spread of SARS-CoV-2.

Lai, C. C., et al. (2020). "Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19): The epidemic and the challenges." Int J Antimicrob Agents **55**(3): 105924.

The emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2; previously provisionally named 2019 novel coronavirus or 2019-nCoV) disease (COVID-19) in China at the end of 2019 has caused a large global outbreak and is a major public health issue. As of 11 February 2020, data from the World Health Organization (WHO) have shown that more than 43 000 confirmed cases have been identified in 28 countries/regions, with >99% of cases being detected in China. On 30 January 2020, the WHO declared COVID-19 as the sixth public health emergency of international concern. SARS-CoV-2 is closely related to two bat-derived severe acute respiratory syndrome-like coronaviruses, bat-SL-

CoVZC45 and bat-SL-CoVZXC21. It is spread by human-to-human transmission via droplets or direct contact, and infection has been estimated to have mean incubation period of 6.4 days and a basic reproduction number of 2.24-3.58. Among patients with pneumonia caused by SARS-CoV-2 (novel coronavirus pneumonia or Wuhan pneumonia), fever was the most common symptom, followed by cough. Bilateral lung involvement with ground-glass opacity was the most common finding from computed tomography images of the chest. The one case of SARS-CoV-2 pneumonia in the USA is responding well to remdesivir, which is now undergoing a clinical trial in China. Currently, controlling infection to prevent the spread of SARS-CoV-2 is the primary intervention being used. However, public health authorities should keep monitoring the situation closely, as the more we can learn about this novel virus and its associated outbreak, the better we can respond.

Lee, N. Y., et al. (2020). "A case of COVID-19 and pneumonia returning from Macau in Taiwan: Clinical course and anti-SARS-CoV-2 IgG dynamic." J Microbiol Immunol Infect.

A 46-year-old woman presented to the emergency department with 2-day fever and cough at seven days after returning from Macau. COVID-19 and pneumonia was diagnosed based on the positive real-time RT-PCR tests for oropharyngeal swab samples and the presence of anti-SARS-COV-2 IgG starting from the illness day 11 and post-exposure 18-21 days.

Letko, M., et al. (2020). "Functional assessment of cell entry and receptor usage for SARS-CoV-2 and other lineage B betacoronaviruses." Nat Microbiol.

Over the past 20 years, several coronaviruses have crossed the species barrier into humans, causing outbreaks of severe, and often fatal, respiratory illness. Since SARS-CoV was first identified in animal markets, global viromics projects have discovered thousands of coronavirus sequences in diverse animals and geographic regions. Unfortunately, there are few tools available to functionally test these viruses for their ability to infect humans, which has severely hampered efforts to predict the next zoonotic viral outbreak. Here, we developed an approach to rapidly screen lineage B betacoronaviruses, such as SARS-CoV and the recent SARS-CoV-2, for receptor usage and their ability to infect cell types from different species. We show that host protease processing during viral entry is a significant barrier for several lineage B viruses and that bypassing this barrier allows several lineage B viruses to enter human cells through an unknown receptor. We also demonstrate how different lineage B viruses can recombine to gain entry into

human cells, and confirm that human ACE2 is the receptor for the recently emerging SARS-CoV-2.

Leung, C. (2020). "The difference in the incubation period of 2019 novel coronavirus (SARS-CoV-2) infection between travelers to Hubei and non-travelers: The need of a longer quarantine period." Infect Control Hosp Epidemiol: 1-8.

Data collected from the individual cases reported by the media were used to estimate the distribution of the incubation period of travelers to Hubei and non-travelers. Upon the finding of longer and more volatile incubation period in travelers, the duration of quarantine should be extended to three weeks.

Li, H., et al. (2020). "Updated approaches against SARS-CoV-2." Antimicrob Agents Chemother.

The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) lies behind the ongoing outbreak of coronavirus disease 2019 (COVID-19). There is a growing understanding of SARS-CoV-2 in the virology, epidemiology and clinical management strategies. However, no anti-SARS-CoV-2 drug or vaccine has been officially approved due to the absence of adequate evidence. Scientists are racing towards the development of treatment for COVID-19. Recent studies have revealed many attractive threptic options, even if some of them remain to be further confirmed in rigorous preclinical models and clinical trials. In this minireview, we aim to summarize the updated potential approaches against SARS-CoV-2. We emphasize that further efforts are warranted to develop the safest and most effective approach.

Li, T. (2020). "Diagnosis and clinical management of severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2) infection: an operational recommendation of Peking Union Medical College Hospital (V2.0)." Emerg Microbes Infect **9**(1): 582-585.

Since December 2019, China has been experiencing an outbreak of a new infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The clinical features include fever, coughing, shortness of breath, and inflammatory lung infiltration. China rapidly listed SARS-CoV-2-related pneumonia as a statutory infectious disease. To standardize the diagnosis and treatment of this new infectious disease, an operational recommendation for the diagnosis and management of SARS-CoV-2 infection is developed by Peking Union Medical College Hospital.

Li, X., et al. (2020). "Evolutionary history, potential intermediate animal host, and cross-species analyses of SARS-CoV-2." J Med Virol.

To investigate the evolutionary history of the recent outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in China, a total of 70 genomes of virus strains from China and elsewhere with sampling dates between 24 December 2019 and 3 February 2020 were analyzed. To explore the potential intermediate animal host of the SARS-CoV-2 virus, we reanalyzed virome data sets from pangolins and representative SARS-related coronaviruses isolates from bats, with particular attention paid to the spike glycoprotein gene. We performed phylogenetic, split network, transmission network, likelihood-mapping, and comparative analyses of the genomes. Based on Bayesian time-scaled phylogenetic analysis using the tip-dating method, we estimated the time to the most recent common ancestor and evolutionary rate of SARS-CoV-2, which ranged from 22 to 24 November 2019 and 1.19 to 1.31 x 10(-3) substitutions per site per year, respectively. Our results also revealed that the BetaCoV/bat/Yunnan/RaTG13/2013 virus was more similar to the SARS-CoV-2 virus than the coronavirus obtained from the two pangolin samples (SRR10168377 and SRR10168378). We also identified a unique peptide (PRRA) insertion in the human SARS-CoV-2 virus, which may be involved in the proteolytic cleavage of the spike protein by cellular proteases, and thus could impact host range and transmissibility. Interestingly, the coronavirus carried by pangolins did not have the RRAR motif. Therefore, we concluded that the human SARS-CoV-2 virus, which is responsible for the recent outbreak of COVID-19, did not come directly from pangolins.

Li, Z., et al. (2020). "Development and Clinical Application of A Rapid IgM-IgG Combined Antibody Test for SARS-CoV-2 Infection Diagnosis." J Med Virol.

The outbreak of the novel coronavirus disease (COVID-19) quickly spread all over China and to more than 20 other countries. Although the virus (SARS-Cov-2) nucleic acid RT-PCR test has become the standard method for diagnosis of SARS-CoV-2 infection, these real-time PCR test kits have many limitations. In addition, high false negative rates were reported. There is an urgent need for an accurate and rapid test method to quickly identify large number of infected patients and asymptomatic carriers to prevent virus transmission and assure timely treatment of patients. We have developed a rapid and simple point-of-care lateral flow immunoassay which can detect IgM and IgG antibodies simultaneously against SARS-CoV-2 virus in human blood within 15 minutes which can detect patients at different infection stages. With this test kit, we carried out clinical studies to validate its clinical efficacy uses. The clinical detection sensitivity and specificity of this test were measured

using blood samples collected from 397 PCR confirmed COVID-19 patients and 128 negative patients at 8 different clinical sites. The overall testing sensitivity was 88.66% and specificity was 90.63%. In addition, we evaluated clinical diagnosis results obtained from different types of venous and fingerstick blood samples. The results indicated great detection consistency among samples from fingerstick blood, serum and plasma of venous blood. The IgM-IgG combined assay has better utility and sensitivity compared with a single IgM or IgG test. It can be used for the rapid screening of SARS-CoV-2 carriers, symptomatic or asymptomatic, in hospitals, clinics, and test laboratories. This article is protected by copyright. All rights reserved.

Lin, L., et al. (2020). "Hypothesis for potential pathogenesis of SARS-CoV-2 infection--a review of immune changes in patients with viral pneumonia." Emerg Microbes Infect: 1-14.

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) with droplets and contact as the main means of transmission. Since the first case appeared in Wuhan, China, in December 2019, the outbreak has gradually spread nationwide. Up to now, according to official data released by the Chinese health commission, the number of newly diagnosed patients has been declining, and the epidemic is gradually being controlled. Although most patients have mild symptoms and good prognosis after infection, some patients developed severe and die from multiple organ complications. The pathogenesis of SARS-CoV-2 infection in humans remains unclear. Immune function is a strong defense against invasive pathogens and there is currently no specific antiviral drug against the virus. This article reviews the immunological changes of coronaviruses like SARS, MERS and other viral pneumonia similar to SARS-CoV-2. Combined with the published literature, the potential pathogenesis of COVID-19 is inferred, and the treatment recommendations for giving high-doses intravenous immunoglobulin and low-molecular-weight heparin anticoagulant therapy to severe type patients are proposed.

Liu, R., et al. (2020). "Positive rate of RT-PCR detection of SARS-CoV-2 infection in 4880 cases from one hospital in Wuhan, China, from Jan to Feb 2020." Clin Chim Acta **505**: 172-175.

BACKGROUND: There's an outbreak of a novel coronavirus (SARS-CoV-2) infection since December 2019, first in China, and currently with more than 80 thousand confirmed infection globally in 29 countries till March 2, 2020. Identification, isolation and caring for patients early are essential to limit human-to-human transmission including reducing secondary infections among close contacts and health care workers, preventing transmission amplification events. The RT-PCR detection of viral nucleic acid test (NAT) was one of the most quickly established laboratory diagnosis method in a novel viral pandemic, just as in this COVID-19 outbreak. METHODS: 4880 cases that had respiratory infection symptoms or close contact with COVID-19 patients in hospital in Wuhan, China, were tested for SARS-CoV-2 infection by use of quantitative RT-PCR (qRT-PCR) on samples from the respiratory tract. Positive rates were calculated in groups divided by genders or ages. RESULTS: The positive rate was about 38% for the total 4880 specimens. Male and older population had a significant higher positive rates. However, 57% was positive among the specimens from the Fever Clinics. Binary logistic regression analysis showed that age, not gender, was the risk factor for SARS-CoV-2 infection in fever clinics. CONCLUSIONS: Therefore, we concluded that viral NAT played an important role in identifying SARS-CoV-2 infection.

Liu, Z., et al. (2020). "Composition and divergence of coronavirus spike proteins and host ACE2 receptors predict potential intermediate hosts of SARS-CoV-2." J Med Virol.

From the beginning of 2002 and 2012, severe respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) crossed the species barriers to infect humans, causing thousands of infections and hundreds of deaths, respectively. Currently, a novel coronavirus (SARS-CoV-2), which has become the cause of the outbreak of Coronavirus Disease 2019 (COVID-19), was discovered. Until 18 February 2020, there were 72 533 confirmed COVID-19 cases (including 10 644 severe cases) and 1872 deaths in China. SARS-CoV-2 is spreading among the public and causing substantial burden due to its human-to-human transmission. However, the intermediate host of SARS-CoV-2 is still unclear. Finding the possible intermediate host of SARS-CoV-2 is imperative to prevent further spread of the epidemic. In this study, we used systematic comparison and analysis to predict the interaction between the receptor-binding domain (RBD) of coronavirus spike protein and the host receptor, angiotensin-converting enzyme 2 (ACE2). The interaction between the key amino acids of S protein RBD and ACE2 indicated that, other than pangolins and snakes, as previously suggested, turtles (Chrysemys picta bellii, Chelonia mydas, and Pelodiscus sinensis) may act as the potential intermediate hosts transmitting SARS-CoV-2 to humans.

Luan, J., et al. (2020). "Spike protein recognition of mammalian ACE2 predicts the host range and an optimized ACE2 for SARS-CoV-2 infection." Biochem Biophys Res Commun.

SARS-CoV-2 causes the recent global COVID-19 public health emergency. ACE2 is the receptor for both SARS-CoV-2 and SARS-CoV. To predict the potential host range of SARS-CoV-2, we analyzed the key residues of ACE2 for recognizing S protein. We found that most of the selected mammals including pets (dog and cat), pangolin and Circetidae mammals remained the most of key residues for association with S protein from SARS-CoV and SARS-CoV-2. The interaction interface between cat/dog/pangolin/Chinese hamster ACE2 and SARS-CoV/SARS-CoV-2 S protein was simulated through homology modeling. We identified that N82 in ACE2 showed a closer contact with SARS-CoV-2 S protein than M82 in human ACE2. Our finding will provide important insights into the host range of SARS-CoV-2 and a new strategy to design an optimized ACE2 for SARS-CoV-2 infection.

Lung, J., et al. (2020). "The potential chemical structure of anti-SARS-CoV-2 RNA-dependent RNA polymerase." J Med Virol.

An outbreak of coronavirus disease 2019 (COVID-19) occurred in Wuhan and it has rapidly spread to almost all parts of the world. For coronaviruses, RNA-dependent RNA polymerase (RdRp) is an important protease that catalyzes the replication of RNA from RNA template and is an attractive therapeutic target. In this study, we screened these chemical structures from traditional Chinese medicinal compounds proven to show antiviral activity in severe acute respiratory syndrome coronavirus (SARS-CoV) and the similar chemical structures through a molecular docking study to target RdRp of SARS-CoV-2, SARS-CoV, and Middle East respiratory syndrome coronavirus (MERS-CoV). We found that theaflavin has a lower idock score in the catalytic pocket of RdRp in SARS-CoV-2 (-9.11 kcal/mol), SARS-CoV (-8.03 kcal/mol), and MERS-CoV (-8.26 kcal/mol) from idock. To confirm the result, we discovered that theaflavin has lower binding energy of -8.8 kcal/mol when it docks in the catalytic pocket of SARS-CoV-2 RdRp by using the Blind Docking server. Regarding contact modes, hydrophobic interactions contribute significantly in binding and additional hydrogen bonds were found between theaflavin and RdRp. Moreover, one pi-cation interaction was formed between theaflavin and Arg553 from the Blind Docking server. Our results suggest that theaflavin could be a potential SARS-CoV-2 RdRp inhibitor for further study.

Marraro, G. A. and C. Spada (2020). "Consideration of the respiratory support strategy of severe acute respiratory failure caused by SARS-CoV-2 infection in children." Zhongguo Dang Dai Er Ke Za Zhi 22(3): 183-194.

The recent ongoing outbreak of severe pneumonia associated with a novel coronavirus (SARS-CoV-2), currently of unknown origin, creates a world emergency that has put global public health institutions on high alert. At present there is limited clinical information of the SARS-CoV-2 and there is no specific treatment recommended, although technical guidances and suggestions have been developed and will continue to be updated as additional information becomes available. Preventive treatment has an important role to control and avoid the spread of severe respiratory disease, but often is difficult to obtain and sometimes cannot be effective to reduce the risk of deterioration of the underlining lung pathology. In order to define an effective and safe treatment for SARS-CoV-2-associated disease, we provide considerations on the actual treatments, on how to avoid complications and the undesirable side effects related to them and to select and apply earlier the most appropriate treatment. Approaching to treat severe respiratory disease in infants and children, the risks related to the development of atelectasis starting invasive or non-invasive ventilation support and the risk of oxygen toxicity must be taken into serious consideration. For an appropriate and effective approach to treat severe pediatric respiratory diseases, two main different strategies can be proposed according to the stage and severity of the patient conditions: patient in the initial phase and with non-severe lung pathology and patient with severe initial respiratory impairment and/or with delay in arrival to observation. The final outcome is strictly connected with the ability to apply an appropriate treatment early and to reduce all the complications that can arise during the intensive care admission.

Matsuyama, S., et al. (2020). "Enhanced isolation of SARS-CoV-2 by TMPRSS2-expressing cells." Proc Natl Acad Sci U S A.

A novel betacoronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which caused a large respiratory outbreak in Wuhan, China in December 2019, is currently spreading across many countries globally. Here, we show that a TMPRSS2-expressing VeroE6 cell line is highly susceptible to SARS-CoV-2 infection, making it useful for isolating and propagating SARS-CoV-2. Our results reveal that, in common with SARS- and Middle East respiratory syndrome-CoV, SARS-CoV-2 infection is enhanced by TMPRSS2.

Medical Association of Chinese People's Liberation, A., et al. (2020). "[Response plan in the neonatal intensive care unit during epidemic of SARS-CoV-2 infection (2nd Edition)]." Zhongguo Dang Dai Er Ke Za Zhi **22**(3): 205-210.

Since December 2019, an outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has spread from China to other countries. In order to effectively respond to possible neonatal SARS-CoV-2 infection, neonatologists from the Medical Association of Chinese People's Liberation Army and the Editorial Committee of Chinese Journal of Contemporary Pediatrics proposed the response plan in the neonatal intensive care unit during epidemic of SARS-CoV-2 infection (1st edition) at the end of January of 2020. Based on the further knowledge and experience on SARS-CoV-2 infection, the neonatologists updated the plan according to the current evidence, so as to provide a better guide for clinical medical staff to deal with the SARS-CoV-2 infection in the NICU.

Neher, R. A., et al. (2020). "Potential impact of seasonal forcing on a SARS-CoV-2 pandemic." Swiss Med Wkly **150**: w20224.

A novel coronavirus (SARS-CoV-2) first detected in Wuhan, China, has spread rapidly since December 2019, causing more than 100,000 confirmed infections and 4000 fatalities (as of 10 March 2020). The outbreak has been declared a pandemic by the WHO on Mar 11, 2020. Here, we explore how seasonal variation in transmissibility could modulate a SARS-CoV-2 pandemic. Data from routine diagnostics show a strong and consistent seasonal variation of the four endemic coronaviruses (229E, HKU1, NL63, OC43) and we parameterise our model for SARS-CoV-2 using these data. The model allows for many subpopulations of different size with variable parameters. Simulations of different scenarios show that plausible parameters result in a small peak in early 2020 in temperate regions of the Northern Hemisphere and a larger peak in winter 2020/2021. Variation in transmission and migration rates can result in substantial variation in prevalence between regions. While the uncertainty in parameters is large, the scenarios we explore show that transient reductions in the incidence rate might be due to a combination of seasonal variation and infection control efforts but do not necessarily mean the epidemic is contained. Seasonal forcing on SARS-CoV-2 should thus be taken into account in the further monitoring of the global transmission. The likely aggregated effect of seasonal variation, infection control measures, and transmission rate variation is a prolonged pandemic wave with lower prevalence at any given time, thereby

providing a window of opportunity for better preparation of health care systems.

Nie, J., et al. (2020). "Establishment and validation of a pseudovirus neutralization assay for SARS-CoV-2." Emerg Microbes Infect **9**(1): 680-686.

Pseudoviruses are useful virological tools because of their safety and versatility, especially for emerging and re-emerging viruses. Due to its high pathogenicity and infectivity and the lack of effective vaccines and therapeutics, live SARS-CoV-2 has to be handled under biosafety level 3 conditions, which has hindered the development of vaccines and therapeutics. Based on a VSV pseudovirus production system, a pseudovirus-based neutralization assay has been developed for evaluating neutralizing antibodies against SARS-CoV-2 in biosafety level 2 facilities. The key parameters for this assay were optimized, including cell types, cell numbers, virus inoculum. When tested against the SARS-CoV-2 pseudovirus, SARS-CoV-2 convalescent patient sera showed high neutralizing potency, which underscore its potential as therapeutics. The limit of detection for this assay was determined as 22.1 and 43.2 for human and mouse serum samples respectively using a panel of 120 negative samples. The cutoff values were set as 30 and 50 for human and mouse serum samples, respectively. This assay showed relatively low coefficient of variations with 15.9% and 16.2% for the intra- and inter-assay analyses respectively. Taken together, we established a robust pseudovirus-based neutralization assay for SARS-CoV-2 and are glad to share pseudoviruses and related protocols with the developers of vaccines or therapeutics to fight against this lethal virus.

Park, W. B., et al. (2020). "Virus Isolation from the First Patient with SARS-CoV-2 in Korea." J Korean Med Sci **35**(7): e84.

Novel coronavirus (SARS-CoV-2) is found to cause a large outbreak started from Wuhan since December 2019 in China and SARS-CoV-2 infections have been reported with epidemiological linkage to China in 25 countries until now. We isolated SARS-CoV-2 from the oropharyngeal sample obtained from the patient with the first laboratory-confirmed SARS-CoV-2 infection in Korea. Cytopathic effects of SARS-CoV-2 in the Vero cell cultures were confluent 3 days after the first blind passage of the sample. Coronavirus was confirmed with spherical particle having a fringe reminiscent of crown on transmission electron microscopy. Phylogenetic analyses of whole genome sequences showed that it clustered with other SARS-CoV-2 reported from Wuhan.

Peyronnet, V., et al. (2020). "[Infection with SARS-CoV-2 in pregnancy. Information and proposed care. CNGOF.]." Gynecol Obstet Fertil Senol.

A new coronavirus (SARS-CoV-2) highlighted at the end of 2019 in China is spreading across all continents. Most often at the origin of a mild infectious syndrome, associating mild symptoms (fever, cough, myalgia, headache and possible digestive disorders) to different degrees, SARS-Covid-2 can cause serious pulmonary pathologies and sometimes death.Data on the consequences during pregnancy are limited. The first Chinese data published seem to show that the symptoms in pregnant women are the same as those of the general population. There are no cases of intrauterine maternal-fetal transmission, but cases of newborns infected early suggest that there could be vertical perpartum or neonatal transmission. Induced prematurity and cases of respiratory distress in newborns of infected mothers have been described.Pregnancy is known as a period at higher risk for the consequences of respiratory infections, as for influenza, so it seems important to screen for Covid-19 in the presence of symptoms and to monitor closely pregnant women.In this context of the SARS-Covid-2 epidemic, the societies of gynecology-obstetrics, infectious diseases and neonatalogy have proposed a French protocol for the management of possible and proven cases of SARS-Covid-2 in pregnant women. These proposals may evolve on a daily basis with the advancement of the epidemic and knowledge in pregnant women. Subsequently, an in-depth analysis of cases in pregnant women will be necessary in order to improve knowledge on the subject.

Pfefferle, S., et al. (2020). "Evaluation of a quantitative RT-PCR assay for the detection of the emerging coronavirus SARS-CoV-2 using a high throughput system." Euro Surveill 25(9).

Facing the emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), high-volume respiratory testing is demanded in laboratories worldwide. We evaluated the performance of a molecular assay for the detection of SARS-CoV-2 on a high-throughput platform, the cobas 6800, using the 'open channel' for integration of a laboratory-developed assay. We observed good analytical performance in clinical specimens. The fully automated workflow enables high-throughput testing with minimal hands-on time, while offering fast and reliable results.

Phan, T. (2020). "Genetic diversity and evolution of SARS-CoV-2." Infect Genet Evol 81: 104260.

COVID-19 is a viral respiratory illness caused by a new coronavirus called SARS-CoV-2. The World Health Organization declared the SARS-CoV-2 outbreak a global public health emergency. We performed genetic analyses of eighty-six complete or near-complete genomes of SARS-CoV-2 and revealed many mutations and deletions on coding and non-coding regions. These observations provided evidence of the genetic diversity and rapid evolution of this novel coronavirus.

Porcheddu, R., et al. (2020). "Similarity in Case Fatality Rates (CFR) of COVID-19/SARS-COV-2 in Italy and China." J Infect Dev Ctries 14(2): 125-128.

As of 28 February 2020, Italy had 888 cases of SARS-CoV-2 infections, with most cases in Northern Italy in the Lombardia and Veneto regions. Travel-related cases were the main source of COVID-19 cases during the early stages of the current epidemic in Italy. The month of February, however, has been dominated by two large clusters of outbreaks in Northern Italy, south of Milan, with mainly local transmission the source of infections. Contact tracing has failed to identify patient zero in one of the outbreaks. As of 28 February 2020, twenty-one cases of COVID-19 have died. Comparison between case fatality rates in China and Italy are identical at 2.3. Additionally, deaths are similar in both countries with fatalities in mostly the elderly with known comorbidities. It will be important to develop point-of-care devices to aid clinicians in stratifying elderly patients as early as possible to determine the potential level of care they will require to improve their chances of survival from COVID-19 disease.

Qiu, Y., et al. (2020). "Predicting the angiotensin converting enzyme 2 (ACE2) utilizing capability as the receptor of SARS-CoV-2." Microbes Infect.

SARS-CoV-2, the newly identified human coronavirus causing severe pneumonia epidemic, was probably originated from Chinese horseshoe bats. However, direct transmission of the virus from bats to humans is unlikely due to lack of direct contact, implying the existence of unknown intermediate hosts. Angiotensin converting enzyme 2 (ACE2) is the receptor of SARS-CoV-2, but only ACE2s of certain species can be utilized by SARS-CoV-2. Here, we evaluated and ranked the receptor-utilizing capability of ACE2s from various species by phylogenetic clustering and sequence alignment with the currently known ACE2s utilized by SARS-CoV-2. As a result, we predicted that SARS-CoV-2 tends to utilize ACE2s of various mammals, except murines, and some birds, such as pigeon. This prediction may help to screen the intermediate hosts of SARS-CoV-2.

Rombola, G., et al. (2020). "Practical indications for the prevention and management of SARS-CoV-2

in ambulatory dialysis patients: lessons from the first phase of the epidemics in Lombardy." J Nephrol.

Confronting the SARS-CoV-2 outbreak has allowed us to appreciate how efficiently highly-resourced settings can respond to crises. However even such settings are not prepared to deal with the situation, and lessons are only slowly being learnt. There is still an urgent need to accelerate protocols that lead to the implementation of rapid point-of-care diagnostic testing and effective antiviral therapies. In some high-risk populations, such as dialysis patients, where several individuals are treated at the same time in a limited space and overcrowded areas, our objective must be to ensure protection to patients, the healthcare team and the dialysis ward. The difficult Italian experience may help other countries to face the challenges. The experience of the Lombardy underlines the need for gathering and sharing our data to increase our knowledge and support common, initially experience-based, and as soon as possible evidence-based position to face this overwhelming crisis.

Roussel, Y., et al. (2020). "SARS-CoV-2: fear versus data." Int J Antimicrob Agents: 105947.

SARS-CoV-2, the novel coronavirus from China, is spreading around the world, causing a huge reaction despite its current low incidence outside China and the Far East. Four common coronaviruses are in current circulation and cause millions of cases worldwide. This article compares the incidence and mortality rates of these four common coronaviruses with those of SARS-COV-2 in Organisation for Economic Co-operation and Development countries. It is concluded that the problem of SARS-CoV-2 is probably being overestimated, as 2.6 million people die of respiratory infections each year compared with less than 4000 deaths for SARS-CoV-2 at the time of writing.

Runfeng, L., et al. (2020). "Lianhuaqingwen exerts anti-viral and anti-inflammatory activity against novel coronavirus (SARS-CoV-2)." Pharmacol Res: 104761.

PURPOSE: Lianhuaqingwen (LH) as traditional Chinese medicine (TCM) formula has been used to treat influenza and exerted broad-spectrum antiviral effects on a series of influenza viruses and immune regulatory effects [1]. The goal of this study is to demonstrate the antiviral activity of LH against the novel SARS-CoV-2 virus and its potential effect in regulating host immune response. METHODS: The antiviral activity of LH against SARS-CoV-2 was assessed in Vero E6 cells using CPE and plaque reduction assay. The effect of LH on virion morphology was visualized under transmission electron microscope. Pro-inflammatory cytokine expression levels upon SARS-CoV-2 infection in Huh-7 cells were measured by real-time quantitative PCR assays. RESULTS: LH significantly inhibited SARS-CoV-2 replication in Vero E6 cells and markedly reduced pro-inflammatory cytokines (TNF-alpha, IL-6, CCL-2/MCP-1 and CXCL-10/IP-10) production at the mRNA levels. Furthermore, LH treatment resulted in abnormal particle morphology of virion in cells. CONCLUSIONS: LH significantly inhibits the SARS-COV-2 replication, affects virus morphology and exerts anti-inflammatory activity in vitro. These findings indicate that LH protects against the virus attack, making its use a novel strategy for controlling the COVID-19 disease.

Sah, R., et al. (2020). "Complete Genome Sequence of a 2019 Novel Coronavirus (SARS-CoV-2) Strain Isolated in Nepal." Microbiol Resour Announc 9(11).

A complete genome sequence was obtained for a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) strain isolated from an oropharyngeal swab specimen of a Nepalese patient with coronavirus disease 2019 (COVID-19), who had returned to Nepal after traveling to Wuhan, China.

Schwartz, D. A. (2020). "An Analysis of 38 Pregnant Women with COVID-19, Their Newborn Infants, and Maternal-Fetal Transmission of SARS-CoV-2: Maternal Coronavirus Infections and Pregnancy Outcomes." Arch Pathol Lab Med.

The emergence of a novel coronavirus, termed SARS-CoV-2, and the potentially life-threating respiratory disease that it can produce, COVID-19, has rapidly spread across the globe creating a massive public health problem. Previous epidemics of many emerging viral infections have typically resulted in poor obstetrical outcomes including maternal morbidity and mortality, maternal-fetal transmission of the virus, and perinatal infections and death. This communication reviews the effects of two previous coronavirus infections - severe acute respiratory syndrome (SARS) caused by SARS-CoV and Middle East respiratory syndrome (MERS) caused by MERS-CoV - on pregnancy outcomes. In addition, it analyzes literature describing 38 pregnant women with COVID-19 and their newborns in China to assess the effects of SARS-CoV-2 on the mothers and infants including clinical, laboratory and virologic data, and the transmissibility of the virus from mother to fetus. This analysis reveals that unlike coronavirus infections of pregnant women caused by SARS and MERS, in these 38 pregnant women COVID-19 did not lead to maternal deaths. Importantly, and similar to pregnancies with SARS and MERS, there were no confirmed cases of intrauterine transmission of SARS-

CoV-2 from mothers with COVID-19 to their fetuses. All neonatal specimens tested, including in some cases placentas, were negative by rt-PCR for SARS-CoV-2. At this point in the global pandemic of COVID-19 infection there is no evidence that SARS-CoV-2 undergoes intrauterine or transplacental transmission from infected pregnant women to their fetuses. Analysis of additional cases is necessary to determine if this remains true.

Shang, W., et al. (2020). "The outbreak of SARS-CoV-2 pneumonia calls for viral vaccines." NPJ Vaccines **5**: 18.

The outbreak of 2019-novel coronavirus disease (COVID-19) that is caused by SARS-CoV-2 has spread rapidly in China, and has developed to be a Public Health Emergency of International Concern. However, no specific antiviral treatments or vaccines are available yet. This work aims to share strategies and candidate antigens to develop safe and effective vaccines against SARS-CoV-2.

Shen, Z., et al. (2020). "Genomic diversity of SARS-CoV-2 in Coronavirus Disease 2019 patients." Clin Infect Dis.

BACKGROUND: A novel coronavirus (SARS-CoV-2) has infected more than 75,000 individuals and spread to over 20 countries. It is still unclear how fast the virus evolved and how the virus interacts with other microorganisms in the lung. METHODS: We have conducted metatranscriptome sequencing for the bronchoalveolar lavage fluid of eight SARS-CoV-2 patients, 25 community-acquired pneumonia (CAP) patients, and 20 healthy controls. RESULTS: The median number of intra-host variants was 1-4 in SARS-CoV-2 infected patients, which ranged between 0 and 51 in different samples. The distribution of variants on genes was similar to those observed in the population data (110 sequences). However, very few intra-host variants were observed in the population as polymorphism, implying either a bottleneck or purifying selection involved in the transmission of the virus, or a consequence of the limited diversity represented in the current polymorphism data. Although current evidence did not support the transmission of intra-host variants in a person-to-person spread, the risk should not be overlooked. The microbiota in SARS-CoV-2 infected patients was similar to those in CAP, either dominated by the pathogens or with elevated levels of oral and upper respiratory commensal bacteria. CONCLUSION: SARS-CoV-2 evolves in vivo after infection, which may affect its virulence, infectivity, and transmissibility. Although how the intra-host variant spreads in the population is still elusive, it is necessary

to strengthen the surveillance of the viral evolution in the population and associated clinical changes.

Sociedad Espanola de Patologia, D. and G. Asociacion Espanola de (2020). "Recommendations by the SEPD and AEG, both in general and on the operation of gastrointestinal endoscopy and gastroenterology units, concerning the current SARS-CoV-2 pandemic (March, 18)." Rev Esp Enferm Dig.

Infection with SARS-CoV-2 coronavirus, and the disease this agent may induce, are a cause of notable concern for the general population and, of course, among our professionals and patients. Gastrointestinal (GI) endoscopy is a high-risk diagnostic-therapeutic procedure in the case of upper GI examinations, and a moderate to low-risk intervention when involving lower GI explorations. The presence of SARS-CoV-2 RNA in the feces of patients infected with the virus, and occasionally in colonic biopsy samples, has been consistently documented. In fact, viral elimination in the feces may be more prolonged than viral identification in respiratory tract secretions. Furthermore, viral transmission may occur in asymptomatic individuals. However, as of this moment no information has been reported on the possibility of viral transmission, even to professionals, via this route.

Sun, P., et al. (2020). "Clinical characteristics of hospitalized patients with SARS-CoV-2 infection: A single arm meta-analysis." J Med Virol.

OBJECTIVE: We aim to summarize reliable evidence of evidence-based medicine for the treatment and prevention of the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) by analyzing all the published studies on the clinical characteristics of patients with SARS-CoV-2. METHODS: PubMed, Cochrane Library, Embase, and other databases were searched. Several studies on the clinical characteristics of SARS-CoV-2 infection were collected for meta-analysis. RESULTS: Ten studies were included in Meta-analysis, including a total number of 50466 patients with SARS-CoV-2 infection. Meta-analysis shows that, among these patients, the incidence of fever was 0.891 (95% CI: 0.818, 0.945), the incidence of cough was 0.722 (95% CI: 0.657, 0.782), and the incidence of muscle soreness or fatigue was 0.425 (95% CI: 0.213, 0.652). The incidence of acute respiratory distress syndrome (ARDS) was 0.148 (95% CI: 0.046, 0.296), the incidence of abnormal chest computer tomography (CT) was 0.966 (95% CI: 0.921, 0.993), the percentage of severe cases in all infected cases was 0.181 (95% CI: 0.127, 0.243), and the case fatality rate of patients with SARS-CoV-2 infection was 0.043 (95% CI: 0.027, 0.061). CONCLUSION: Fever and cough are the most common symptoms in patients with

SARS-CoV-2 infection, and most of these patients have abnormal chest CT examination. Several people have muscle soreness or fatigue as well as ARDS. Diarrhea, hemoptysis, headache, sore throat, shock, and other symptoms are rare. The case fatality rate of patients with SARS-CoV-2 infection is lower than that of Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS). This meta-analysis also has limitations, so the conclusions of this Meta-analysis still need to be verified by more relevant studies with more careful design, more rigorous execution, and larger sample size.

Ton, A. T., et al. (2020). "Rapid Identification of Potential Inhibitors of SARS-CoV-2 Main Protease by Deep Docking of 1.3 Billion Compounds." Mol Inform.

The recently emerged 2019 Novel Coronavirus (SARS-CoV-2) and associated COVID-19 disease cause serious or even fatal respiratory tract infection and yet no approved therapeutics or effective treatment is currently available to effectively combat the outbreak. This urgent situation is pressing the world to respond with the development of novel vaccine or a small molecule therapeutics for SARS-CoV-2. Along these efforts, the structure of SARS-CoV-2 main protease (Mpro) has been rapidly resolved and made publicly available to facilitate global efforts to develop novel drug candidates. Recently, our group has developed a novel deep learning platform - Deep Docking (DD) which provides fast prediction of docking scores of Glide (or any other docking program) and, hence, enables structure-based virtual screening of billions of purchasable molecules in a short time. In the current study we applied DD to all 1.3 billion compounds from ZINC15 library to identify top 1,000 potential ligands for SARS-CoV-2 Mpro protein. The compounds are made publicly available for further characterization and development by scientific community.

Tong, Z. D., et al. (2020). "Potential Presymptomatic Transmission of SARS-CoV-2, Zhejiang Province, China, 2020." Emerg Infect Dis **26**(5).

We report a 2-family cluster of persons infected with severe acute respiratory syndrome coronavirus 2 in the city of Zhoushan, Zhejiang Province, China, during January 2020. The infections resulted from contact with an infected but potentially presymptomatic traveler from the city of Wuhan in Hubei Province.

Touzard-Romo, F., et al. (2020). "Co-infection with SARS-CoV-2 and Human Metapneumovirus." R I Med J (2013) **103**(2): 75-76.

The novel coronavirus (now called SARS-CoV-2) initially discovered in Wuhan, China, has now become a global pandemic. We describe a patient presenting to an Emergency Department in Rhode Island on March 12, 2020 with cough and shortness of breath after a trip to Jamaica. The patient underwent nasopharyngeal swab for a respiratory pathogen panel as well as SARS-CoV-2 RT-PCR. When the respiratory pathogen panel was positive for human metapneumovirus, the patient was treated and discharged. SARS-CoV-2 RT-PCR came back positive 24 hours later. Although respiratory viral co-infection is thought to be relatively uncommon in adults, this case reflects that SARS-CoV-2 testing algorithms that exclude patients who test positive for routine viral pathogens may miss SARS-CoV-2 co-infected patients.

Walls, A. C., et al. (2020). "Structure, Function, and Antigenicity of the SARS-CoV-2 Spike Glycoprotein." Cell.

The emergence of SARS-CoV-2 has resulted in >90,000 infections and >3,000 deaths. Coronavirus spike (S) glycoproteins promote entry into cells and are the main target of antibodies. We show that SARS-CoV-2 S uses ACE2 to enter cells and that the receptor-binding domains of SARS-CoV-2 S and SARS-CoV S bind with similar affinities to human ACE2, correlating with the efficient spread of SARS-CoV-2 among humans. We found that the SARS-CoV-2 S glycoprotein harbors a furin cleavage site at the boundary between the S1/S2 subunits, which is processed during biogenesis and sets this virus apart from SARS-CoV and SARS-related CoVs. We determined cryo-EM structures of the SARS-CoV-2 S ectodomain trimer, providing a blueprint for the design of vaccines and inhibitors of viral entry. Finally, we demonstrate that SARS-CoV S murine polyclonal antibodies potently inhibited SARS-CoV-2 S mediated entry into cells, indicating that cross-neutralizing antibodies targeting conserved S epitopes can be elicited upon vaccination.

Wang, C., et al. (2020). "The establishment of reference sequence for SARS-CoV-2 and variation analysis." J Med Virol.

Starting around December 2019, an epidemic of pneumonia, which was named COVID-19 by the World Health Organization, broke out in Wuhan, China, and is spreading throughout the world. A new coronavirus, named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by the Coronavirus Study Group of the International Committee on Taxonomy of Viruses was soon found to be the cause. At present, the sensitivity of clinical nucleic acid detection is limited, and it is still unclear whether it is related to genetic variation. In this study, we retrieved

95 full-length genomic sequences of SARAS-CoV-2 strains from the National Center for Biotechnology Information and GISAID databases, established the reference sequence by conducting multiple sequence alignment and phylogenetic analyses, and analyzed sequence variations along the SARS-CoV-2 genome. The homology among all viral strains was generally high, among them, 99.99% (99.91%-100%) at the nucleotide level and 99.99% (99.79%-100%) at the amino acid level. Although overall variation in open-reading frame (ORF) regions is low, 13 variation sites in 1a, 1b, S, 3a, M, 8, and N regions were identified, among which positions nt28144 in ORF 8 and nt8782 in ORF 1a showed mutation rate of 30.53% (29/95) and 29.47% (28/95), respectively. These findings suggested that there may be selective mutations in SARS-COV-2, and it is necessary to avoid certain regions when designing primers and probes. Establishment of the reference sequence for SARS-CoV-2 could benefit not only biological study of this virus but also diagnosis, clinical monitoring and intervention of SARS-CoV-2 infection in the future.

Wang, J., et al. (2020). "[SARS-CoV-2 infection with gastrointestinal symptoms as the first manifestation in a neonate]." Zhongguo Dang Dai Er Ke Za Zhi **22**(3): 211-214.

Since December 2019, the outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has occurred in Wuhan, Hubei Province, China. The infected cases were noted mostly in adults, but rarely reported in children, especially neonates. Most children with SARS-CoV-2 infection present mainly with respiratory symptoms, but less commonly with gastrointestinal symptoms, and tend to have mild clinical symptoms. A neonate with SARS-CoV-2 infection, who had vomiting and milk refusal as the first symptom, was recently admitted to Wuhan Children's Hospital. After two weeks of treatment, the patient recovered gradually and was discharged. Here, this case is reported to improve the understanding of SARS-CoV-2 infection in neonates.

Wang, L. S., et al. (2020). "[An interpretation on perinatal and neonatal management plan for prevention and control of SARS-CoV-2 infection (2nd Edition)]." Zhongguo Dang Dai Er Ke Za Zhi **22**(3): 199-204.

The epidemic of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection continues so far. The cases of SARS-CoV-2 infection have been reported in pregnant women and neonates as special groups. Perinatal and neonatal management plan for prevention and control of SARS-CoV-2 infection (2nd Edition) has been worked out by the Editorial Committee of Chinese Journal of Contemporary Pediatrics. This paper presents an interpretation on the 2nd Edition of the management plan, so as to facilitate readers to better understand it.

Wang, X., et al. (2020). "Challenges to the system of reserve medical supplies for public health emergencies: reflections on the outbreak of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) epidemic in China." Biosci Trends **14**(1): 3-8.

On December 31, 2019, the Wuhan Municipal Health Commission announced an outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), China is now at a critical period in the control of the epidemic. The Chinese Government has been taking a series of rapid, comprehensive, and effective prevention and control measures. As the pandemic has developed, a fact has become apparent: there is a serious dearth of emergency medical supplies, and especially an extreme shortage of personal protective equipment such as masks and medical protective clothing. This is one of the major factors affecting the progress of epidemic prevention and control. Although China has made great efforts to strengthen the ability to quickly respond to public health emergencies since the SARS outbreak in 2003 and it has clarified requirements for emergency supplies through legislation, the emergency reserve supplies program has not been effectively implemented, and there are also deficiencies in the types, quantity, and availability of emergency medical supplies. A sound system of emergency reserve supplies is crucial to the management of public health emergencies. Based on international experiences with pandemic control, the world should emphasize improving the system of emergency reserve medical supplies in the process of establishing and improving public health emergency response systems, and it should promote the establishment of international cooperative programs to jointly deal with public health emergencies of international concern in the future.

Wassenaar, T. M. and Y. Zou (2020). "2019_nCoV/SARS-CoV-2: rapid classification of betacoronaviruses and identification of Traditional Chinese Medicine as potential origin of zoonotic coronaviruses." Lett Appl Microbiol.

The current outbreak of a novel severe acute respiratory syndrome-like coronavirus, 2019_nCoV (now named SARS-CoV-2), illustrated difficulties in identifying a novel coronavirus and its natural host, as the coding sequences of various Betacoronavirus species can be highly diverse. By means of whole-genome sequence comparisons, we demonstrate that the noncoding flanks of the viral genome can be used to correctly separate the recognized four betacoronavirus subspecies. The conservation would

be sufficient to define target sequences that could, in theory, classify novel virus species into their subspecies. Only 253 upstream noncoding sequences of Sarbecovirus are sufficient to identify genetic similarities between species of this subgenus. Furthermore, it was investigated which bat species have commercial value in China, and would thus likely be handled for trading purposes. A number of coronavirus genomes have been published that were obtained from such bat species. These bats are used in Traditional Chinese Medicine, and their handling poses a potential risk to cause zoonotic coronavirus epidemics. SIGNIFICANCE AND IMPACT OF THE STUDY: The noncoding upstream and downstream flanks of coronavirus genomes allow for rapid classification of novel Betacoronavirus species and correct identification of genetic relationships. Although bats are the likely natural host of 2019_nCoV, the exact bat species that serves as the natural host of the virus remains as yet unknown. Chinese bat species with commercial value were identified as natural reservoirs of coronaviruses and are used in Traditional Chinese Medicine. Since their trading provides a potential risk for spreading zoonoses, a change in these practices is highly recommended.

Won, J., et al. (2020). "Development of a Laboratory-safe and Low-cost Detection Protocol for SARS-CoV-2 of the Coronavirus Disease 2019 (COVID-19)." Exp Neurobiol.

The severe acute respiratory coronavirus 2 (SARS-CoV-2), which emerged in December 2019 in Wuhan, China, has spread rapidly to over a dozen countries. Especially, the spike of case numbers in South Korea sparks pandemic worries. This virus is reported to spread mainly through personto- person contact via respiratory droplets generated by coughing and sneezing, or possibly through surface contaminated by people coughing or sneezing on them. More critically, there have been reports about the possibility of this virus to transmit even before a virus-carrying person to show symptoms. Therefore, a low-cost, easy-access protocol for early detection of this virus is desperately needed. Here, we have established a real-time reverse-transcription PCR (rtPCR)-based assay protocol composed of easy specimen self-collection from a subject via pharyngeal swab, Trizolbased RNA purification, and SYBR Green-based rtPCR. This protocol shows an accuracy and sensitivity limit of 1-10 virus particles as we tested with a known lentivirus. The cost for each sample is estimated to be less than 15 US dollars. Overall time it takes for an entire protocol is estimated to be less than 4 hours. We propose a cost-effective, quick-and-easy method for early detection of SARS-CoV-2 at any

conventional Biosafety Level II laboratories that are equipped with a rtPCR machine. Our newly developed protocol should be helpful for a first-hand screening of the asymptomatic virus-carriers for further prevention of transmission and early intervention and treatment for the rapidly propagating virus.

Working Group for the, P. and S.-C.-I. i. t. P. P. o. t. E. C. o. C. J. o. C. P. Control of Neonatal (2020). "[Perinatal and neonatal management plan for prevention and control of SARS-CoV-2 infection (2nd Edition)]." Zhongguo Dang Dai Er Ke Za Zhi **22**(3): 195-198.

Since late December 2019, SARS-CoV-2 infection has spread to all parts of the country and overseas, and the outbreak continues. At the end of January 2020, the Working Group for the Prevention and Control of Neonatal SARS-CoV-2 Infection in the Perinatal Period of the Editorial Committee of Chinese Journal of Contemporary Pediatrics worked out the perinatal and neonatal management plan for prevention and control of SARS-CoV-2 infection (1st Edition). This plan has been verified by clinical practice for 3 weeks. With the further understanding of SARS-CoV-2 infection, especially the emergence of SARS-CoV-2 infection cases in pregnant women and neonates, it is necessary to update the first edition of the management plan so as to offer a better guide on clinical practice. Therefore, the Working Group has worked out the second edition of the management plan.

Wu, D., et al. (2020). "The SARS-CoV-2 outbreak: what we know." Int J Infect Dis.

There is a current worldwide outbreak of the novel coronavirus Covid-19 (coronavirus disease 2019; the pathogen called SARS-CoV-2; previously 2019-nCoV), which originated from Wuhan in China and has now spread to 6 continents including 66 countries, as of 24:00 on March 2, 2020. Governments are under increased pressure to stop the outbreak spiraling into a global health emergency. At this stage, preparedness, transparency, and sharing of information are crucial to risk assessments and beginning outbreak control activities. This information should include reports from outbreak site and from laboratories supporting the investigation. This paper aggregates and consolidates the epidemiology, clinical manifestations, diagnosis, treatments and preventions of this new type of coronavirus.

Wu, X., et al. (2020). "Co-infection with SARS-CoV-2 and Influenza A Virus in Patient with Pneumonia, China." Emerg Infect Dis **26**(6).

We report co-infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and influenza A virus in a patient with pneumonia in

China. The case highlights possible co-detection of known respiratory viruses. We noted low sensitivity of upper respiratory specimens for SARS-CoV-2, which could further complicate recognition of the full extent of disease.

Xia, J., et al. (2020). "Evaluation of coronavirus in tears and conjunctival secretions of patients with SARS-CoV-2 infection." J Med Virol.

OBJECTIVE: This study aimed to assess the presence of novel coronavirus in tears and conjunctival secretions of SARS-CoV-2-infected patients. METHODS: A prospective interventional case series study was performed, and 30 confirmed novel coronavirus pneumonia (NCP) patients were selected at the First Affiliated Hospital of Zhejiang University from 26 January 2020 to 9 February 2020. At an interval of 2 to 3 days, tear and conjunctival secretions were collected twice with disposable sampling swabs for reverse-transcription polymerase chain reaction (RT-PCR) assay. RESULTS: Twenty-one common-type and nine severe-type NCP patients were enrolled. Two samples of tear and conjunctival secretions were obtained from the only one patient with conjunctivitis yielded positive RT-PCR results. Fifty-eight samples from other patents were all negative. CONCLUSION: We speculate that SARS-CoV-2 may be detected in the tears and conjunctival secretions in NCP patients with conjunctivitis.

Xu, J., et al. (2020). "Systematic Comparison of Two Animal-to-Human Transmitted Human Coronaviruses: SARS-CoV-2 and SARS-CoV." Viruses **12**(2).

After the outbreak of the severe acute respiratory syndrome (SARS) in the world in 2003, human coronaviruses (HCoVs) have been reported as pathogens that cause severe symptoms in respiratory tract infections. Recently, a new emerged HCoV isolated from the respiratory epithelium of unexplained pneumonia patients in the Wuhan seafood market caused a major disease outbreak and has been named the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). This virus causes acute lung symptoms, leading to a condition that has been named as "coronavirus disease 2019" (COVID-19). The emergence of SARS-CoV-2 and of SARS-CoV caused widespread fear and concern and has threatened global health security. There are some similarities and differences in the epidemiology and clinical features between these two viruses and diseases that are caused by these viruses. The goal of this work is to systematically review and compare between SARS-CoV and SARS-CoV-2 in the context of their virus incubation, originations, diagnosis and

treatment methods, genomic and proteomic sequences, and pathogenic mechanisms.

Xu, X., et al. (2020). "Imaging and clinical features of patients with 2019 novel coronavirus SARS-CoV-2." Eur J Nucl Med Mol Imaging.

BACKGROUND: The pneumonia caused by the 2019 novel coronavirus (SARS-CoV-2, also called 2019-nCoV) recently break out in Wuhan, China, and was named as COVID-19. With the spread of the disease, similar cases have also been confirmed in other regions of China. We aimed to report the imaging and clinical characteristics of these patients infected with SARS-CoV-2 in Guangzhou, China. METHODS: All patients with laboratory-identified SARS-CoV-2 infection by real-time polymerase chain reaction (PCR) were collected between January 23, 2020, and February 4, 2020, in a designated hospital (Guangzhou Eighth People's Hospital). This analysis included 90 patients (39 men and 51 women; median age, 50 years (age range, 18-86 years). All the included SARS-CoV-2-infected patients underwent non-contrast enhanced chest computed tomography (CT). We analyzed the clinical characteristics of the patients, as well as the distribution characteristics, pattern, morphology, and accompanying manifestations of lung lesions. In addition, after 1-6 days (mean 3.5 days), follow-up chest CT images were evaluated to assess radiological evolution. FINDINGS: The majority of infected patients had a history of exposure in Wuhan or to infected patients and mostly presented with fever and cough. More than half of the patients presented bilateral, multifocal lung lesions, with peripheral distribution, and 53 (59%) patients had more than two lobes involved. Of all included patients, COVID-19 pneumonia presented with ground glass opacities in 65 (72%), consolidation in 12 (13%), crazy paving pattern in 11 (12%), interlobular thickening in 33 (37%), adjacent pleura thickening in 50 (56%), and linear opacities combined in 55 (61%). Pleural effusion, pericardial effusion, and lymphadenopathy were uncommon findings. In addition, baseline chest CT did not show any abnormalities in 21 patients (23%), but 3 patients presented bilateral ground glass opacities on the second CT after 3-4 days. CONCLUSION: SARS-CoV-2 infection can be confirmed based on the patient's history, clinical manifestations, imaging characteristics, and laboratory tests. Chest CT examination plays an important role in the initial diagnosis of the novel coronavirus pneumonia. Multiple patchy ground glass opacities in bilateral multiple lobular with periphery distribution are typical chest CT imaging features of the COVID-19 pneumonia.

Xu, X. W., et al. (2020). "Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-Cov-2) outside of Wuhan, China: retrospective case series." BMJ **368**: m606.

OBJECTIVE: To study the clinical characteristics of patients in Zhejiang province, China, infected with the 2019 severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2) responsible for coronavirus disease 2019 (covid-2019). DESIGN: Retrospective case series. SETTING: Seven hospitals in Zhejiang province, China. PARTICIPANTS: 62 patients admitted to hospital with laboratory confirmed SARS-Cov-2 infection. Data were collected from 10 January 2020 to 26 January 2020. MAIN OUTCOME MEASURES: Clinical data, collected using a standardised case report form, such as temperature, history of exposure, incubation period. If information was not clear, the working group in Hangzhou contacted the doctor responsible for treating the patient for clarification. RESULTS: Of the 62 patients studied (median age 41 years), only one was admitted to an intensive care unit, and no patients died during the study. According to research, none of the infected patients in Zhejiang province were ever exposed to the Huanan seafood market, the original source of the virus; all studied cases were infected by human to human transmission. The most common symptoms at onset of illness were fever in 48 (77%) patients, cough in 50 (81%), expectoration in 35 (56%), headache in 21 (34%), myalgia or fatigue in 32 (52%), diarrhoea in 3 (8%), and haemoptysis in 2 (3%). Only two patients (3%) developed shortness of breath on admission. The median time from exposure to onset of illness was 4 days (interquartile range 3-5 days), and from onset of symptoms to first hospital admission was 2 (1-4) days. CONCLUSION: As of early February 2020, compared with patients initially infected with SARS-Cov-2 in Wuhan, the symptoms of patients in Zhejiang province are relatively mild.

Xu, Y. H., et al. (2020). "Clinical and computed tomographic imaging features of novel coronavirus pneumonia caused by SARS-CoV-2." J Infect **80**(4): 394-400.

PURPOSE: To investigate the clinical and imaging characteristics of computed tomography (CT) in novel coronavirus pneumonia (NCP) caused by SARS-CoV-2. MATERIALS AND METHODS: A retrospective analysis was performed on the imaging findings of patients confirmed with COVID-19 pneumonia who had chest CT scanning and treatment after disease onset. The clinical and imaging data were analyzed. RESULTS: Fifty patients were enrolled, including mild type in nine, common in 28, severe in 10 and critically severe in the rest three. Mild patients (29 years) were significantly (P<0.03) younger than either common (44.5 years) or severe (54.7) and critically severe (65.7 years) patients, and common patients were also significantly (P<0.03) younger than severe and critically severe patients. Mild patients had low to moderate fever (<39.1 degrees C), 49 (98%) patients had normal or slightly reduced leukocyte count, 14 (28%) had decreased counts of lymphocytes, and 26 (52%) patients had increased C-reactive protein. Nine mild patients were negative in CT imaging. For all the other types of NCP, the lesion was in the right upper lobe in 30 cases, right middle lobe in 22, right lower lobe in 39, left upper lobe in 33 and left lower lobe in 36. The lesion was primarily located in the peripheral area under the pleura with possible extension towards the pulmonary hilum. Symmetrical lesions were seen in 26 cases and asymmetrical in 15. The density of lesion was mostly uneven with ground glass opacity as the primary presentation accompanied by partial consolidation and fibrosis. CONCLUSION: CT imaging presentations of NCP are mostly patchy ground glass opacities in the peripheral areas under the pleura with partial consolidation which will be absorbed with formation of fibrotic stripes if improved. CT scanning provides important bases for early diagnosis and treatment of NCP.

Yan, R., et al. (2020). "Structural basis for the recognition of the SARS-CoV-2 by full-length human ACE2." Science.

Angiotensin-converting enzyme 2 (ACE2) is the cellular receptor for SARS coronavirus (SARS-CoV) and the new coronavirus (SARS-CoV-2) that is causing the serious epidemic COVID-19. Here we present cryo-EM structures of full-length human ACE2, in the presence of a neutral amino acid transporter B (0)AT1, with or without the receptor binding domain (RBD) of the surface spike glycoprotein (S protein) of SARS-CoV-2, both at an overall resolution of 2.9 A, with a local resolution of 3.5 A at the ACE2-RBD interface. The ACE2-B (0)AT1 complex is assembled as a dimer of heterodimers, with the Collectrin-like domain (CLD) of ACE2 mediating homo-dimerization. The RBD is recognized by the extracellular peptidase domain (PD) of ACE2 mainly through polar residues. These findings provide important insights to the molecular basis for coronavirus recognition and infection.

Yang, X., et al. (2020). "Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study." Lancet Respir Med.

BACKGROUND: An ongoing outbreak of pneumonia associated with the severe acute respiratory coronavirus 2 (SARS-CoV-2) started in December, 2019, in Wuhan, China. Information about critically ill

patients with SARS-CoV-2 infection is scarce. We aimed to describe the clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia. METHODS: In this single-centered, retrospective, observational study, we enrolled 52 critically ill adult patients with SARS-CoV-2 pneumonia who were admitted to the intensive care unit (ICU) of Wuhan Jin Yin-tan hospital (Wuhan, China) between late December, 2019, and Jan 26, 2020. Demographic data, symptoms, laboratory values, comorbidities, treatments, and clinical outcomes were all collected. Data were compared between survivors and non-survivors. The primary outcome was 28-day mortality, as of Feb 9, 2020. Secondary outcomes included incidence of SARS-CoV-2-related acute respiratory distress syndrome (ARDS) and the proportion of patients requiring mechanical ventilation. FINDINGS: Of 710 patients with SARS-CoV-2 pneumonia, 52 critically ill adult patients were included. The mean age of the 52 patients was 59.7 (SD 13.3) years, 35 (67%) were men, 21 (40%) had chronic illness, 51 (98%) had fever. 32 (61.5%) patients had died at 28 days, and the median duration from admission to the intensive care unit (ICU) to death was 7 (IQR 3-11) days for non-survivors. Compared with survivors, non-survivors were older (64.6 years [11.2] vs 51.9 years [12.9]), more likely to develop ARDS (26 [81%] patients vs 9 [45%] patients), and more likely to receive mechanical ventilation (30 [94%] patients vs 7 [35%] patients), either invasively or non-invasively. Most patients had organ function damage, including 35 (67%) with ARDS, 15 (29%) with acute kidney injury, 12 (23%) with cardiac injury, 15 (29%) with liver dysfunction, and one (2%) with pneumothorax. 37 (71%) patients required mechanical ventilation. Hospital-acquired infection occurred in seven (13.5%) patients. INTERPRETATION: The mortality of critically ill patients with SARS-CoV-2 pneumonia is considerable. The survival time of the non-survivors is likely to be within 1-2 weeks after ICU admission. Older patients (>65 years) with comorbidities and ARDS are at increased risk of death. The severity of SARS-CoV-2 pneumonia poses great strain on critical care resources in hospitals, especially if they are not adequately staffed or resourced. FUNDING: None.

Yao, X., et al. (2020). "In Vitro Antiviral Activity and Projection of Optimized Dosing Design of Hydroxychloroquine for the Treatment of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)." Clin Infect Dis.
BACKGROUND: The Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) first broke out in Wuhan (China) and subsequently spread worldwide. Chloroquine has been sporadically used in treating SARS-CoV-2 infection. Hydroxychloroquine

shares the same mechanism of action as chloroquine, but its more tolerable safety profile makes it the preferred drug to treat malaria and autoimmune conditions. We propose that the immunomodulatory effect of hydroxychloroquine also may be useful in controlling the cytokine storm that occurs late-phase in critically ill SARS-CoV-2 infected patients. Currently, there is no evidence to support the use of hydroxychloroquine in SARS-CoV-2 infection. METHODS: The pharmacological activity of chloroquine and hydroxychloroquine was tested using SARS-CoV-2 infected Vero cells. Physiologically-based pharmacokinetic models (PBPK) were implemented for both drugs separately by integrating their in vitro data. Using the PBPK models, hydroxychloroquine concentrations in lung fluid were simulated under 5 different dosing regimens to explore the most effective regimen whilst considering the drug's safety profile. RESULTS: Hydroxychloroquine (EC50=0.72 muM) was found to be more potent than chloroquine (EC50=5.47 muM) in vitro. Based on PBPK models results, a loading dose of 400 mg twice daily of hydroxychloroquine sulfate given orally, followed by a maintenance dose of 200 mg given twice daily for 4 days is recommended for SARS-CoV-2 infection, as it reached three times the potency of chloroquine phosphate when given 500 mg twice daily 5 days in advance. CONCLUSIONS: Hydroxychloroquine was found to be more potent than chloroquine to inhibit SARS-CoV-2 in vitro.

Young, B. E., et al. (2020). "Epidemiologic Features and Clinical Course of Patients Infected With SARS-CoV-2 in Singapore." JAMA.
Importance: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in Wuhan, China, in December 2019 and has spread globally with sustained human-to-human transmission outside China. Objective: To report the initial experience in Singapore with the epidemiologic investigation of this outbreak, clinical features, and management. Design, Setting, and Participants: Descriptive case series of the first 18 patients diagnosed with polymerase chain reaction (PCR)-confirmed SARS-CoV-2 infection at 4 hospitals in Singapore from January 23 to February 3, 2020; final follow-up date was February 25, 2020. Exposures: Confirmed SARS-CoV-2 infection. Main Outcomes and Measures: Clinical, laboratory, and radiologic data were collected, including PCR cycle threshold values from nasopharyngeal swabs and viral shedding in blood, urine, and stool. Clinical course was summarized, including requirement for supplemental oxygen and intensive care and use of empirical treatment with lopinavir-ritonavir. Results: Among the 18 hospitalized patients with PCR-confirmed SARS-CoV-2 infection (median age, 47

years; 9 [50%] women), clinical presentation was an upper respiratory tract infection in 12 (67%), and viral shedding from the nasopharynx was prolonged for 7 days or longer among 15 (83%). Six individuals (33%) required supplemental oxygen; of these, 2 required intensive care. There were no deaths. Virus was detectable in the stool (4/8 [50%]) and blood (1/12 [8%]) by PCR but not in urine. Five individuals requiring supplemental oxygen were treated with lopinavir-ritonavir. For 3 of the 5 patients, fever resolved and supplemental oxygen requirement was reduced within 3 days, whereas 2 deteriorated with progressive respiratory failure. Four of the 5 patients treated with lopinavir-ritonavir developed nausea, vomiting, and/or diarrhea, and 3 developed abnormal liver function test results. Conclusions and Relevance: Among the first 18 patients diagnosed with SARS-CoV-2 infection in Singapore, clinical presentation was frequently a mild respiratory tract infection. Some patients required supplemental oxygen and had variable clinical outcomes following treatment with an antiretroviral agent.

Yuen, K. S., et al. (2020). "SARS-CoV-2 and COVID-19: The most important research questions." Cell Biosci 10: 40.

Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is an ongoing global health emergency. Here we highlight nine most important research questions concerning virus transmission, asymptomatic and presymptomatic virus shedding, diagnosis, treatment, vaccine development, origin of virus and viral pathogenesis.

Zhang, G. X., et al. (2020). "[Twin girls infected with SARS-CoV-2]." Zhongguo Dang Dai Er Ke Za Zhi 22(3): 221-225.

This article reports the diagnosis and treatment of twin girls who were diagnosed with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in Hunan Province, China. The twin girls, aged 1 year and 2 months, were admitted on January 29, 2020 due to fever for one day and cough and sneezing for two days respectively. Both recovered after symptomatic treatment. The two girls had mild symptoms and rapid recovery, suggesting that children with SARS-CoV-2 infection may be mild and have a good prognosis. There were differences in the clinical symptoms and imaging findings between the twin girls, suggesting that SARS-CoV-2 infection has diverse clinical features in children.

Zhang, J. F., et al. (2020). "SARS-CoV-2 turned positive in a discharged patient with COVID-19

arouses concern regarding the present standard for discharge." Int J Infect Dis.

An outbreak of COVID-19 in Wuhan, China caused by SARS-CoV-2 has led to a serious epidemic in China and other countries, resulting in worldwide concern. With the active efforts from prevention and control, the quantity of discharged patients is escalating. How to manage these patients normatively is still challenging. We hereby reported an asymptomatic discharged patient with COVID-19 who was retested positive for SARS-CoV-2, which arouses concern regarding the present discharge standard of COVID-19.

Zhang, J. J., et al. (2020). "Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China." Allergy.

BACKGROUND: Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has been widely spread. We aim to investigate the clinical characteristic and allergy status of patients infected with SARS-CoV-2. METHODS: Electronic medical records including demographics, clinical manifestation, comorbidities, laboratory data, and radiological materials of 140 hospitalized COVID-19 patients, with confirmed result of SARS-CoV-2 viral infection, were extracted and analyzed. RESULTS: An approximately 1:1 ratio of male (50.7%) and female COVID-19 patients was found, with an overall median age of 57.0 years. All patients were community-acquired cases. Fever (91.7%), cough (75.0%), fatigue (75.0%), and gastrointestinal symptoms (39.6%) were the most common clinical manifestations, whereas hypertension (30.0%) and diabetes mellitus (12.1%) were the most common comorbidities. Drug hypersensitivity (11.4%) and urticaria (1.4%) were self-reported by several patients. Asthma or other allergic diseases were not reported by any of the patients. Chronic obstructive pulmonary disease (COPD, 1.4%) patients and current smokers (1.4%) were rare. Bilateral ground-glass or patchy opacity (89.6%) was the most common sign of radiological finding. Lymphopenia (75.4%) and eosinopenia (52.9%) were observed in most patients. Blood eosinophil counts correlate positively with lymphocyte counts in severe (r =.486, P <.001) and nonsevere (r =.469, P <.001) patients after hospital admission. Significantly higher levels of D-dimer, C-reactive protein, and procalcitonin were associated with severe patients compared to nonsevere patients (all P <.001). CONCLUSION: Detailed clinical investigation of 140 hospitalized COVID-19 cases suggests eosinopenia together with lymphopenia may be a potential indicator for diagnosis. Allergic diseases, asthma, and COPD are not risk factors for SARS-CoV-2 infection. Older age, high number of

comorbidities, and more prominent laboratory abnormalities were associated with severe patients.

Zhang, L., et al. (2020). "Crystal structure of SARS-CoV-2 main protease provides a basis for design of improved alpha-ketoamide inhibitors." <u>Science</u>.

The COVID-19 pandemic caused by SARS-CoV-2 is a global health emergency. An attractive drug target among coronaviruses is the main protease (M (pro), 3CL (pro)), due to its essential role in processing the polyproteins that are translated from the viral RNA. We report the X-ray structures of the unliganded SARS-CoV-2 M (pro) and its complex with an alpha-ketoamide inhibitor. This was derived from a previously designed inhibitor but with the P3-P2 amide bond incorporated into a pyridone ring to enhance the half-life of the compound in plasma. Based on the structure, we developed the lead compound into a potent inhibitor of the SARS-CoV-2 M (pro) The pharmacokinetic characterization of the optimized inhibitor reveals a pronounced lung tropism and suitability for administration by the inhalative route.

Zhang, T., et al. (2020). "Probable Pangolin Origin of SARS-CoV-2 Associated with the COVID-19 Outbreak." <u>Curr Biol</u>.

An outbreak of coronavirus disease 2019 (COVID-19) caused by the 2019 novel coronavirus (SARS-CoV-2) began in the city of Wuhan in China and has widely spread worldwide. Currently, it is vital to explore potential intermediate hosts of SARS-CoV-2 to control COVID-19 spread. Therefore, we reinvestigated published data from pangolin lung samples from which SARS-CoV-like CoVs were detected by Liu et al. [1]. We found genomic and evolutionary evidence of the occurrence of a SARS-CoV-2-like CoV (named Pangolin-CoV) in dead Malayan pangolins. Pangolin-CoV is 91.02% and 90.55% identical to SARS-CoV-2 and BatCoV RaTG13, respectively, at the whole-genome level. Aside from RaTG13, Pangolin-CoV is the most closely related CoV to SARS-CoV-2. The S1 protein of Pangolin-CoV is much more closely related to SARS-CoV-2 than to RaTG13. Five key amino acid residues involved in the interaction with human ACE2 are completely consistent between Pangolin-CoV and SARS-CoV-2, but four amino acid mutations are present in RaTG13. Both Pangolin-CoV and RaTG13 lost the putative furin recognition sequence motif at S1/S2 cleavage site that can be observed in the SARS-CoV-2. Conclusively, this study suggests that pangolin species are a natural reservoir of SARS-CoV-2-like CoVs.

Zhang, X., et al. (2020). "Epidemiological, clinical characteristics of cases of SARS-CoV-2 infection with abnormal imaging findings." <u>Int J Infect Dis</u>.

PURPOSE: To investigate the epidemiological, clinical characteristics of COVID-19 patients with abnormal imaging findings. METHODS: Patients confirmed with SARS-CoV-2 infection of Zhejiang province from Jan 17 to Feb 8 underwent CT or x-ray were enrolled. Epidemiological, clinical data were analyzed between those with abnormal or normal imaging findings. RESULTS: Excluding 72 patients with normal images, 230 of 573 patients affected more than two lobes. The median radiograph score was 2.0 and there's negative correlation between the score and oxygenation index (rho=-0.657,P < 0.001). Patients with abnormal images were older (46.65 +/- 13.82), with higher rate of coexisting condition (28.8%), lower rate of exposure history and longer time between onset and confirmation (5d) than non-pneumonia patients (all P < 0.05). Higher rate of fever, cough, expectoration, and headache, lower lymphocytes, albumin, serum sodium levels and higher total bilirubin, creatine kinase, lactate dehydrogenase and C-reactive protein levels and lower oxygenation index were observed in pneumonia patients (all P < 0.05). Muscle ache, shortness of breath, nausea and vomiting, lower lymphocytes levels and higher serum creatinine and radiograph score at admission were predictive factors for severe/critical subtype. CONCLUSION: Patients with abnormal images have more obvious clinical manifestations and laboratory changes. Combing clinical features and radiograph score can effectively predict severe/critical type.

Zhou, Y., et al. (2020). "Network-based drug repurposing for novel coronavirus 2019-nCoV/SARS-CoV-2." <u>Cell Discov</u> **6**: 14.

Human coronaviruses (HCoVs), including severe acute respiratory syndrome coronavirus (SARS-CoV) and 2019 novel coronavirus (2019-nCoV, also known as SARS-CoV-2), lead global epidemics with high morbidity and mortality. However, there are currently no effective drugs targeting 2019-nCoV/SARS-CoV-2. Drug repurposing, representing as an effective drug discovery strategy from existing drugs, could shorten the time and reduce the cost compared to de novo drug discovery. In this study, we present an integrative, antiviral drug repurposing methodology implementing a systems pharmacology-based network medicine platform, quantifying the interplay between the HCoV-host interactome and drug targets in the human protein-protein interaction network. Phylogenetic analyses of 15 HCoV whole genomes reveal that 2019-nCoV/SARS-CoV-2 shares the highest nucleotide sequence identity with SARS-CoV (79.7%).

Specifically, the envelope and nucleocapsid proteins of 2019-nCoV/SARS-CoV-2 are two evolutionarily conserved regions, having the sequence identities of 96% and 89.6%, respectively, compared to SARS-CoV.

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