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# COVID-19 and ACE2 Research Literatures

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**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.
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**Key words**: COVID-19; America; 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.

Baig, A. M., et al. (2020). "Evidence of the COVID-19 Virus Targeting the CNS: Tissue Distribution, Host-Virus Interaction, and Proposed Neurotropic Mechanisms." ACS Chem Neurosci.

The recent outbreak of coronavirus infectious disease 2019 (COVID-19) has gripped the world with apprehension and has evoked a scare of epic proportion regarding its potential to spread and infect humans worldwide. As we are in the midst of an ongoing pandemic of COVID-19, scientists are struggling to understand how it resembles and differs from the severe acute respiratory syndrome coronavirus (SARS-CoV) at the genomic and transcriptomic level. In a short time following the outbreak, it has been shown that, similar to SARS-CoV, COVID-19 virus exploits the angiotensin-converting enzyme 2 (ACE2) receptor to gain entry inside the cells. This finding raises the curiosity of investigating the expression of ACE2 in neurological tissue and determining the possible contribution of neurological tissue damage to the morbidity and mortality caused by COIVD-19. Here, we investigate the density of the expression levels of ACE2 in the CNS, the host-virus interaction and relate it to the pathogenesis and complications seen in the recent cases resulting from the COVID-19 outbreak. Also, we debate the need for a model for staging COVID-19 based on neurological tissue involvement.

Batlle, D., et al. (2020). "Soluble angiotensin-converting enzyme 2: a potential approach for coronavirus infection therapy?" Clin Sci (Lond) **134**(5): 543-545.

A new coronavirus, referred to as SARS-CoV-2, is responsible for the recent outbreak of severe respiratory disease. This outbreak first detected in Wuhan, China in December 2019, has spread to other regions of China and to 25 other countries as of January, 2020. It has been known since the 2003 SARS epidemic that the receptor critical for SARS-CoV entry into host cells is the angiotensin-converting enzyme 2 (ACE2). The S1 domain of the spike protein of SARS-CoV attaches the virus to its cellular receptor ACE2 on the host cells. We thought that it is timely to explain the connection between the SARS-CoV, SARS-CoV-2, ACE2 and the rationale for soluble ACE2 as a potential therapy.

Chen, J. (2020). "Pathogenicity and transmissibility of 2019-nCoV-A quick overview and comparison with other emerging viruses." Microbes Infect **22**(2): 69-71.

A zoonotic coronavirus, tentatively labeled as 2019-nCoV by the World Health Organization (WHO), has been identified as the causative agent of the viral pneumonia outbreak in Wuhan, China, at the end of 2019. Although 2019-nCoV can cause a severe respiratory illness like SARS and MERS, evidence from clinics suggested that 2019-nCoV is generally less pathogenic than SARS-CoV, and much less than MERS-CoV. The transmissibility of 2019-nCoV is still debated and needs to be further assessed. To avoid the 2019-nCoV outbreak turning into an epidemic or even a pandemic and to minimize the mortality rate, China activated emergency response procedures, but much remains to be learned about the features of the virus to refine the risk assessment and response. Here, the current knowledge in 2019-nCoV pathogenicity and transmissibility is summarized in comparison with several commonly known emerging viruses, and information urgently needed for a better control of the disease is highlighted.

Diaz, J. H. (2020). "Hypothesis: angiotensin-converting enzyme inhibitors and angiotensin receptor blockers may increase the risk of severe COVID-19." J Travel Med.

Intravenous infusions of angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) in experimental animals increase the numbers of angiotensin-converting enzyme 2 (ACE2) receptors in the cardiopulmonary circulation. ACE2 receptors serve as binding sites for SARS-CoV-2 virions in the lungs. Patients who take ACEIs and ARBS may be at increased risk of severe disease outcomes due to SARS-CoV-2 infections.

Fan, H. H., et al. (2020). "Repurposing of clinically approved drugs for treatment of coronavirus disease 2019 in a 2019-novel coronavirus (2019-nCoV) related coronavirus model." Chin Med J (Engl).

BACKGROUND: Medicines for the treatment of 2019-novel coronavirus (2019-nCoV) infections are urgently needed. However, drug screening using live 2019-nCoV requires high-level biosafety facilities, which imposes an obstacle for those without such facilities or 2019-novel coronavirus (2019-nCoV). This study aims to repurpose the clinically approved drugs for the treatment of coronavirus disease 2019 (COVID-19) in a 2019-nCoV related coronavirus model. METHODS: A 2019-nCoV related pangolin coronavirus GX_P2V/pangolin/2017/ Guangxi was described. Whether GX_P2X uses angiotensin-converting enzyme 2 (ACE2) as the cell receptor was investigated by using small interfering RNA (siRNA) - mediated silencing of ACE2. The pangolin coronavirus model was used to identify drug candidates for treating 2019-nCoV infection. Two libraries of 2406 clinically approved drugs were screened for their ability to inhibit cytopathic effects on Vero E6 cells by GX_P2X infection. The antiviral activities and antiviral mechanisms of potential drugs were further investigated. Viral yields of RNAs and infectious particles were quantified by quantitative real-time polymerase chain reaction (qRT-PCR) and plaque assay, respectively. RESULTS: The spike protein of coronavirus GX_P2V shares 92.2% amino acid identity with that of 2019-nCoV isolate Wuhan-hu-1, and uses ACE2 as the receptor for infection just like 2019-nCoV. Three drugs-cepharanthine (CEP), selamectin and mefloquine hydrochloride exhibited complete inhibition of cytopathic effects in cell culture at 10 mumol/L. CEP demonstrated the most potent inhibition of GX_P2V infection, with a concentration for 50% of maximal effect [EC50] of 0.98 mumol/L. The viral RNA yield in cells treated with 10 mumol/L CEP was 15,393-fold lower than in cells without CEP treatment ([6.48 +/- 0.02] x 10vs. 1.00 +/- 0.12, $t = 150.38$, $P < 0.001$) at 72 h post-infection (p.i.). Plaque assays found no production of live viruses in media containing 10 mumol/L CEP at 48 h p.i. Furthermore, we found CEP has potent antiviral activities against both viral entry (1.00 +/- 0.37 vs. 0.46 +/- 0.12, $t = 2.42$, $P < 0.05$) and viral replication (1.00 +/- 0.43 vs. [6.18 +/- 0.95] x 10, $t = 3.98$, $P < 0.05$). CONCLUSIONS: Our pangolin coronavirus GX_P2V is a workable model for 2019-nCoV research. CEP, selamectin and mefloquine hydrochloride are potential drugs for treating 2019-nCoV infection. Our results strongly suggest that CEP is a wide-spectrum inhibitor

of pan-betacoronavirus, and clinical trial of CEP for treatment of 2019-nCoV infection is warranted.

Fedson, D. S., et al. (2020). "Hiding in Plain Sight: an Approach to Treating Patients with Severe COVID-19 Infection." mBio **11**(2).

Patients with COVID-19 infection are at risk of acute respiratory disease syndrome (ARDS) and death. The tissue receptor for COVID-19 is ACE2, and higher levels of ACE2 can protect against ARDS. Angiotensin receptor blockers and statins upregulate ACE2. Clinical trials are needed to determine whether this drug combination might be used to treat patients with severe COVID-19 infection.

Guo, Y. R., et al. (2020). "The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak - an update on the status." Mil Med Res **7**(1): 11.

An acute respiratory disease, caused by a novel coronavirus (SARS-CoV-2, previously known as 2019-nCoV), the coronavirus disease 2019 (COVID-19) has spread throughout China and received worldwide attention. On 30 January 2020, World Health Organization (WHO) officially declared the COVID-19 epidemic as a public health emergency of international concern. The emergence of SARS-CoV-2, since the severe acute respiratory syndrome coronavirus (SARS-CoV) in 2002 and Middle East respiratory syndrome coronavirus (MERS-CoV) in 2012, marked the third introduction of a highly pathogenic and large-scale epidemic coronavirus into the human population in the twenty-first century. As of 1 March 2020, a total of 87,137 confirmed cases globally, 79,968 confirmed in China and 7169 outside of China, with 2977 deaths (3.4%) had been reported by WHO. Meanwhile, several independent research groups have identified that SARS-CoV-2 belongs to beta-coronavirus, with highly identical genome to bat coronavirus, pointing to bat as the natural host. The novel coronavirus uses the same receptor, angiotensin-converting enzyme 2 (ACE2) as that for SARS-CoV, and mainly spreads through the respiratory tract. Importantly, increasingly evidence showed sustained human-to-human transmission, along with many exported cases across the globe. The clinical symptoms of COVID-19 patients include fever, cough, fatigue and a small population of patients appeared gastrointestinal infection symptoms. The elderly and people with underlying diseases are susceptible to infection and prone to serious outcomes, which may be associated with acute respiratory distress syndrome (ARDS) and cytokine storm. Currently, there are few specific antiviral strategies, but several potent candidates of antivirals and repurposed drugs are under urgent investigation. In this review, we summarized the latest research progress of the epidemiology, pathogenesis, and clinical characteristics of COVID-19, and discussed the current treatment and scientific advancements to combat the epidemic novel coronavirus.

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.

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.

Kannan, S., et al. (2020). "COVID-19 (Novel Coronavirus 2019) - recent trends." Eur Rev Med Pharmacol Sci **24**(4): 2006-2011.

The World Health Organization (WHO) has issued a warning that, although the 2019 novel coronavirus (COVID-19) from Wuhan City (China), is not pandemic, it should be contained to prevent the global spread. The COVID-19 virus was known earlier as 2019-nCoV. As of 12 February 2020, WHO reported 45,171 cases and 1115 deaths related to COVID-19. COVID-19 is similar to Severe Acute Respiratory Syndrome coronavirus (SARS-CoV) virus in its pathogenicity, clinical spectrum, and epidemiology. Comparison of the genome sequences of COVID-19, SARS-CoV, and Middle East Respiratory Syndrome coronavirus (MERS-CoV) showed that COVID-19 has a better sequence identity with SARS-CoV compared to MERS CoV. However, the amino acid sequence of COVID-19 differs from other coronaviruses specifically in the regions of 1ab polyprotein and surface glycoprotein or S-protein. Although several animals have been speculated to be a reservoir for COVID-19, no animal reservoir has been already confirmed. COVID-19 causes COVID-19 disease that has similar symptoms as SARS-CoV. Studies suggest that the human receptor for COVID-19 may be angiotensin-converting enzyme 2 (ACE2) receptor similar to that of SARS-CoV. The nucleocapsid (N) protein of COVID-19 has nearly 90% amino acid sequence identity with SARS-CoV. The N protein antibodies of SARS-CoV may cross react with COVID-19 but may not provide cross-immunity. In a similar fashion to SARS-CoV, the N protein of COVID-19 may play an important role in suppressing the RNA interference (RNAi) to overcome the host defense. This mini-review aims at investigating the most recent trend of COVID-19.

Kruse, R. L. (2020). "Therapeutic strategies in an outbreak scenario to treat the novel coronavirus originating in Wuhan, China." F1000Res **9**: 72.

A novel coronavirus (2019-nCoV) originating in Wuhan, China presents a potential respiratory viral pandemic to the world population. Current efforts are focused on containment and quarantine of infected individuals. Ultimately, the outbreak could be controlled with a protective vaccine to prevent 2019-nCoV infection. While vaccine research should be pursued intensely, there exists today no therapy to treat 2019-nCoV upon infection, despite an urgent need to find options to help these patients and preclude potential death. Herein, I review the potential options to treat 2019-nCoV in patients, with an emphasis on the necessity for speed and timeliness in developing new and effective therapies in this outbreak. I consider the options of drug repurposing, developing neutralizing monoclonal antibody therapy, and an oligonucleotide strategy targeting the viral RNA genome, emphasizing the promise and pitfalls of these approaches. Finally, I advocate for the fastest strategy to develop a treatment now, which could be resistant to any mutations the virus may have in the future. The proposal is a biologic that blocks 2019-nCoV entry using a soluble version of the viral receptor, angiotensin-converting enzyme 2 (ACE2), fused to an immunoglobulin Fc domain, providing a neutralizing antibody with maximal breath to avoid any viral escape, while also helping to recruit the immune system to build lasting immunity. The sequence of the ACE2-Fc protein is provided to investigators, allowing its possible use in recombinant protein expression systems to start producing drug today to treat patients under compassionate use, while formal clinical trials are later undertaken. Such a treatment could help infected patients before a protective vaccine is developed and widely available in the coming months to year (s).

Li, J. Y., et al. (2020). "The epidemic of 2019-novel-coronavirus (2019-nCoV) pneumonia and insights for emerging infectious diseases in the future." Microbes Infect **22**(2): 80-85.

At the end of December 2019, a novel coronavirus, 2019-nCoV, caused an outbreak of pneumonia spreading from Wuhan, Hubei province, to the whole country of China, which has posed great threats to public health and attracted enormous attention around the world. To date, there are no clinically approved vaccines or antiviral drugs available for these human coronavirus infections. Intensive research on the novel emerging human infectious coronaviruses is urgently needed to elucidate their route of transmission and pathogenic mechanisms, and to identify potential drug targets, which would promote the development of effective preventive and therapeutic countermeasures. Herein, we describe the epidemic and etiological characteristics of 2019-nCoV, discuss its essential biological features, including tropism and receptor usage, summarize approaches for disease prevention and treatment, and speculate on the transmission route of 2019-nCoV.

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.

Morse, J. S., et al. (2020). "Learning from the Past: Possible Urgent Prevention and Treatment Options for Severe Acute Respiratory Infections Caused by 2019-nCoV." Chembiochem **21**(5): 730-738.

With the current trajectory of the 2019-nCoV outbreak unknown, public health and medicinal measures will both be needed to contain spreading of the virus and to optimize patient outcomes. Although little is known about the virus, an examination of the genome sequence shows strong homology with its better-studied cousin, SARS-CoV. The spike protein used for host cell infection shows key nonsynonymous mutations that might hamper the efficacy of previously developed therapeutics but remains a viable target for the development of biologics and macrocyclic peptides. Other key drug targets, including RNA-dependent RNA polymerase and coronavirus main proteinase (3CLpro), share a strikingly high (>95 %) homology to SARS-CoV. Herein, we suggest four potential drug candidates (an ACE2-based peptide, remdesivir, 3CLpro-1 and a novel vinylsulfone protease inhibitor) that could be used to treat patients suffering with the 2019-nCoV. We also summarize previous efforts into drugging these targets and hope to help in the development of broad-spectrum anti-coronaviral agents for future epidemics.

Olds, J. L. and N. Kabbani (2020). "Is nicotine exposure linked to cardiopulmonary vulnerability to COVID-19 in the general population?" FEBS J.

The recent emergence of COVID-19 has resulted in a worldwide crisis, with large populations locked down and transportation links severed. While approximately 80% of infected individuals have minimal symptoms, around 15-20% need to be hospitalized, greatly stressing global health care systems. As of March 10, the death rate appears to be about 3.4%, although this number is highly stratified among different populations. Here, we focus on those individuals who have been exposed to nicotine prior to their exposure to the virus. We predict that these individuals are "primed" to be at higher risk because nicotine can directly impact the putative receptor for the virus (ACE2) and lead to deleterious signaling in lung epithelial cells.

Peng, X., et al. (2020). "Transmission routes of 2019-nCoV and controls in dental practice." Int J Oral Sci **12**(1): 9.

A novel beta-coronavirus (2019-nCoV) caused severe and even fetal pneumonia explored in a seafood market of Wuhan city, Hubei province, China, and rapidly spread to other provinces of China and other countries. The 2019-nCoV was different from SARS-CoV, but shared the same host receptor the human angiotensin-converting enzyme 2 (ACE2). The natural host of 2019-nCoV may be the bat Rhinolophus affinis

as 2019-nCoV showed 96.2% of whole-genome identity to BatCoV RaTG13. The person-to-person transmission routes of 2019-nCoV included direct transmission, such as cough, sneeze, droplet inhalation transmission, and contact transmission, such as the contact with oral, nasal, and eye mucous membranes. 2019-nCoV can also be transmitted through the saliva, and the fetal-oral routes may also be a potential person-to-person transmission route. The participants in dental practice expose to tremendous risk of 2019-nCoV infection due to the face-to-face communication and the exposure to saliva, blood, and other body fluids, and the handling of sharp instruments. Dental professionals play great roles in preventing the transmission of 2019-nCoV. Here we recommend the infection control measures during dental practice to block the person-to-person transmission routes in dental clinics and hospitals.

Sun, M. L., et al. (2020). "[Inhibitors of RAS Might Be a Good Choice for the Therapy of COVID-19 Pneumonia]." Zhonghua Jie He He Hu Xi Za Zhi **43**(3): 219-222.

The novel coronavirus 2019 (COVID-19) infected patients by binding human ACE2, leading to severe pneumonia and highly mortality rate in patients. At present, there is no definite and effective treatment for COVID-19. ACE2 plays an important role in the RAS, and the imbalance between ACE/Ang II/AT1R pathway and ACE2/Ang (1-7)/Mas receptor pathway in the RAS system will lead to multi-system inflammation. Increased ACE and Ang II are poor prognostic factors for severe pneumonia. Animal studies have shown that RAS inhibitors could effectively relieve symptoms of acute severe pneumonia and respiratory failure. The binding of COVID-19 and ACE2 resulted in the exhaustion of ACE2, and then ACE2/Ang (1-7)/Mas receptor pathway was inhibited. The balance of the RAS system was broken, and this would lead to the exacerbation of acute severe pneumonia. Therefore, we speculate that ACEI and AT1R inhibitors could be used in patients with COVID-19 pneumonia under the condition of controlling blood pressure, and might reduce the pulmonary inflammatory response and mortality.

Sun, M. L., et al. (2020). "[Inhibitors of RAS Might Be a Good Choice for the Therapy of COVID-19 Pneumonia]." Zhonghua Jie He He Hu Xi Za Zhi **43**(0): E014.

The novel coronavirus 2019 (COVID-19) infected patients by binding human ACE2, leading to severe pneumonia and highly mortality rate in patients. At present, there is no definite and effective treatment for COVID-19. ACE2 plays an important role in the RAS, and the imbalance between ACE/Ang II/AT1R pathway and ACE2/Ang (1-7)/Mas receptor pathway in the RAS system will lead to multi-system inflammation. Increased ACE and Ang II are poor prognostic factors for severe pneumonia. Animal studies have shown that RAS inhibitors could effectively relieve symptoms of acute severe pneumonia and respiratory failure. The binding of COVID-19 and ACE2 resulted in the exhaustion of ACE2, and then ACE2/Ang (1-7)/Mas receptor pathway was inhibited. The balance of the RAS system was broken, and this would lead to the exacerbation of acute severe pneumonia. Therefore, we speculate that ACEI and AT1R inhibitors could be used in patients with COVID-19 pneumonia under the condition of controlling blood pressure, and might reduce the pulmonary inflammatory response and mortality.

Sun, Z., et al. (2020). "Potential Factors Influencing Repeated SARS Outbreaks in China." Int J Environ Res Public Health **17**(5).

Within last 17 years two widespread epidemics of severe acute respiratory syndrome (SARS) occurred in China, which were caused by related coronaviruses (CoVs): SARS-CoV and SARS-CoV-2. Although the origin (s) of these viruses are still unknown and their occurrences in nature are mysterious, some general patterns of their pathogenesis and epidemics are noticeable. Both viruses utilize the same receptor-angiotensin-converting enzyme 2 (ACE2)-for invading human bodies. Both epidemics occurred in cold dry winter seasons celebrated with major holidays, and started in regions where dietary consumption of wildlife is a fashion. Thus, if bats were the natural hosts of SARS-CoVs, cold temperature and low humidity in these times might provide conducive environmental conditions for prolonged viral survival in these regions concentrated with bats. The widespread existence of these bat-carried or -released viruses might have an easier time in breaking through human defenses when harsh winter makes human bodies more vulnerable. Once succeeding in making some initial human infections, spreading of the disease was made convenient with increased social gathering and holiday travel. These natural and social factors influenced the general progression and trajectory of the SARS epidemiology. However, some unique factors might also contribute to the origination of SARS in Wuhan. These factors are discussed in different scenarios in order to promote more research for achieving final validation.

Tai, W., et al. (2020). "Characterization of the receptor-binding domain (RBD) of 2019 novel coronavirus: implication for development of RBD

protein as a viral attachment inhibitor and vaccine." Cell Mol Immunol.

The outbreak of Coronavirus Disease 2019 (COVID-19) has posed a serious threat to global public health, calling for the development of safe and effective prophylactics and therapeutics against infection of its causative agent, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), also known as 2019 novel coronavirus (2019-nCoV). The CoV spike (S) protein plays the most important roles in viral attachment, fusion and entry, and serves as a target for development of antibodies, entry inhibitors and vaccines. Here, we identified the receptor-binding domain (RBD) in SARS-CoV-2 S protein and found that the RBD protein bound strongly to human and bat angiotensin-converting enzyme 2 (ACE2) receptors. SARS-CoV-2 RBD exhibited significantly higher binding affinity to ACE2 receptor than SARS-CoV RBD and could block the binding and, hence, attachment of SARS-CoV-2 RBD and SARS-CoV RBD to ACE2-expressing cells, thus inhibiting their infection to host cells. SARS-CoV RBD-specific antibodies could cross-react with SARS-CoV-2 RBD protein, and SARS-CoV RBD-induced antisera could cross-neutralize SARS-CoV-2, suggesting the potential to develop SARS-CoV RBD-based vaccines for prevention of SARS-CoV-2 and SARS-CoV infection.

Tian, H. Y. (2020). "[2019-nCoV: new challenges from coronavirus]." Zhonghua Yu Fang Yi Xue Za Zhi **54**(3): 235-238.

The outbreak of pneumonia caused by the novel coronavirus (2019-nCoV) in Wuhan, Hubei province of China, at the end of 2019 shaped tremendous challenges to China's public health and clinical treatment. The virus belongs to the beta genus Coronavirus in the family Corornaviridae, and is closely related to SARS-CoV and MERS-CoV, causing severe symptoms of pneumonia. The virus is transmitted through droplets, close contact, and other means, and patients in the incubation period could potentially transmit the virus to other persons. According to current observations, 2019-nCoV is weaker than SARS in pathogenesis, but has stronger transmission competence; it's mechanism of cross-species spread might be related with angiotensin-converting enzyme (ACE2), which is consistent with the receptor SARS-CoV. After the outbreak of this disease, Chinese scientists invested a lot of energy to carry out research by developing rapid diagnostic reagents, identifying the characters of the pathogen, screening out clinical drugs that may inhibit the virus, and are rapidly developing vaccines. The emergence of 2019-nCoV reminds us once again of the importance of establishing a systematic coronavirus surveillance network. It also poses new challenges to prevention and control of the emerging epidemic and rapidly responses on scientific research.

Tian, X., et al. (2020). "Potent binding of 2019 novel coronavirus spike protein by a SARS coronavirus-specific human monoclonal antibody." Emerg Microbes Infect **9**(1): 382-385.

The newly identified 2019 novel coronavirus (2019-nCoV) has caused more than 11,900 laboratory-confirmed human infections, including 259 deaths, posing a serious threat to human health. Currently, however, there is no specific antiviral treatment or vaccine. Considering the relatively high identity of receptor-binding domain (RBD) in 2019-nCoV and SARS-CoV, it is urgent to assess the cross-reactivity of anti-SARS CoV antibodies with 2019-nCoV spike protein, which could have important implications for rapid development of vaccines and therapeutic antibodies against 2019-nCoV. Here, we report for the first time that a SARS-CoV-specific human monoclonal antibody, CR3022, could bind potently with 2019-nCoV RBD (KD of 6.3 nM). The epitope of CR3022 does not overlap with the ACE2 binding site within 2019-nCoV RBD. These results suggest that CR3022 may have the potential to be developed as candidate therapeutics, alone or in combination with other neutralizing antibodies, for the prevention and treatment of 2019-nCoV infections. Interestingly, some of the most potent SARS-CoV-specific neutralizing antibodies (e.g. m396, CR3014) that target the ACE2 binding site of SARS-CoV failed to bind 2019-nCoV spike protein, implying that the difference in the RBD of SARS-CoV and 2019-nCoV has a critical impact for the cross-reactivity of neutralizing antibodies, and that it is still necessary to develop novel monoclonal antibodies that could bind specifically to 2019-nCoV RBD.

Wan, Y., et al. (2020). "Receptor Recognition by the Novel Coronavirus from Wuhan: an Analysis Based on Decade-Long Structural Studies of SARS Coronavirus." J Virol **94**(7).

Recently, a novel coronavirus (2019-nCoV) has emerged from Wuhan, China, causing symptoms in humans similar to those caused by severe acute respiratory syndrome coronavirus (SARS-CoV). Since the SARS-CoV outbreak in 2002, extensive structural analyses have revealed key atomic-level interactions between the SARS-CoV spike protein receptor-binding domain (RBD) and its host receptor angiotensin-converting enzyme 2 (ACE2), which regulate both the cross-species and human-to-human transmissions of SARS-CoV. Here, we analyzed the potential receptor usage by 2019-nCoV, based on the rich knowledge about SARS-CoV and the newly

released sequence of 2019-nCoV. First, the sequence of 2019-nCoV RBD, including its receptor-binding motif (RBM) that directly contacts ACE2, is similar to that of SARS-CoV, strongly suggesting that 2019-nCoV uses ACE2 as its receptor. Second, several critical residues in 2019-nCoV RBM (particularly Gln493) provide favorable interactions with human ACE2, consistent with 2019-nCoV's capacity for human cell infection. Third, several other critical residues in 2019-nCoV RBM (particularly Asn501) are compatible with, but not ideal for, binding human ACE2, suggesting that 2019-nCoV has acquired some capacity for human-to-human transmission. Last, while phylogenetic analysis indicates a bat origin of 2019-nCoV, 2019-nCoV also potentially recognizes ACE2 from a diversity of animal species (except mice and rats), implicating these animal species as possible intermediate hosts or animal models for 2019-nCoV infections. These analyses provide insights into the receptor usage, cell entry, host cell infectivity and animal origin of 2019-nCoV and may help epidemic surveillance and preventive measures against 2019-nCoV.IMPORTANCE The recent emergence of Wuhan coronavirus (2019-nCoV) puts the world on alert. 2019-nCoV is reminiscent of the SARS-CoV outbreak in 2002 to 2003. Our decade-long structural studies on the receptor recognition by SARS-CoV have identified key interactions between SARS-CoV spike protein and its host receptor angiotensin-converting enzyme 2 (ACE2), which regulate both the cross-species and human-to-human transmissions of SARS-CoV. One of the goals of SARS-CoV research was to build an atomic-level iterative framework of virus-receptor interactions to facilitate epidemic surveillance, predict species-specific receptor usage, and identify potential animal hosts and animal models of viruses. Based on the sequence of 2019-nCoV spike protein, we apply this predictive framework to provide novel insights into the receptor usage and likely host range of 2019-nCoV. This study provides a robust test of this reiterative framework, providing the basic, translational, and public health research communities with predictive insights that may help study and battle this novel 2019-nCoV.

Xu, H., et al. (2020). "High expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa." Int J Oral Sci **12**(1): 8.

It has been reported that ACE2 is the main host cell receptor of 2019-nCoV and plays a crucial role in the entry of virus into the cell to cause the final infection. To investigate the potential route of 2019-nCov infection on the mucosa of oral cavity, bulk RNA-seq profiles from two public databases including The Cancer Genome Atlas (TCGA) and Functional Annotation of The Mammalian Genome Cap Analysis of Gene Expression (FANTOM5 CAGE) dataset were collected. RNA-seq profiling data of 13 organ types with para-carcinoma normal tissues from TCGA and 14 organ types with normal tissues from FANTOM5 CAGE were analyzed in order to explore and validate the expression of ACE2 on the mucosa of oral cavity. Further, single-cell transcriptomes from an independent data generated in-house were used to identify and confirm the ACE2-expressing cell composition and proportion in oral cavity. The results demonstrated that the ACE2 expressed on the mucosa of oral cavity. Interestingly, this receptor was highly enriched in epithelial cells of tongue. Preliminarily, those findings have explained the basic mechanism that the oral cavity is a potentially high risk for 2019-nCoV infectious susceptibility and provided a piece of evidence for the future prevention strategy in dental clinical practice as well as daily life.

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.

Yen, M. Y., et al. (2020). "Interrupting COVID-19 transmission by implementing enhanced traffic control bundling: Implications for global prevention and control efforts." J Microbiol Immunol Infect.

We argue that enhanced Traffic Control Bundling (eTCB) can interrupt the community-hospital-community transmission cycle, thereby limiting COVID-19's impact. Enhanced TCB is an expansion of the traditional TCB that proved highly effective during Taiwan's 2003 SARS outbreak. TCB's success derived from ensuring that Health Care Workers (HCWs) and patients were protected from fomite, contact and droplet transmission within hospitals. Although TCB proved successful during SARS, achieving a similar level of success with the COVID-

19 outbreak requires adapting TCB to the unique manifestations of this new disease. These manifestations include asymptomatic infection, a hyper-affinity to ACE2 receptors resulting in high transmissibility, false negatives, and an incubation period of up to 22 days. Enhanced TCB incorporates the necessary adaptations. In particular, eTCB includes expanding the TCB transition zone to incorporate a new sector - the quarantine ward. This ward houses patients exhibiting atypical manifestations or awaiting definitive diagnosis. A second adaptation involves enhancing the checkpoint hand disinfection and gowning up with Personal Protective Equipment deployed in traditional TCB. Under eTCB, checkpoint hand disinfection and donning of face masks are now required of all visitors who seek to enter hospitals. These enhancements ensure that transmissions by droplets, fomites and contact are disrupted both within hospitals and between hospitals and the broader community. Evidencing eTCB effectiveness is Taiwan's success to date in containing and controlling the community-hospital-community transmission cycle.

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

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.

Zhou, P., et al. (2020). "A pneumonia outbreak associated with a new coronavirus of probable bat origin." Nature **579**(7798): 270-273.

Since the outbreak of severe acute respiratory syndrome (SARS) 18 years ago, a large number of SARS-related coronaviruses (SARSr-CoVs) have been discovered in their natural reservoir host, bats (1-4). Previous studies have shown that some bat SARSr-CoVs have the potential to infect humans (5-7). Here we report the identification and characterization of a new coronavirus (2019-nCoV), which caused an epidemic of acute respiratory syndrome in humans in Wuhan, China. The epidemic, which started on 12 December 2019, had caused 2,794 laboratory-confirmed infections including 80 deaths by 26 January 2020. Full-length genome sequences were obtained from five patients at an early stage of the outbreak. The sequences are almost identical and share 79.6% sequence identity to SARS-CoV. Furthermore, we show that 2019-nCoV is 96% identical at the whole-genome level to a bat coronavirus. Pairwise protein sequence analysis of seven conserved non-structural proteins domains show that this virus belongs to the species of SARSr-CoV. In addition, 2019-nCoV virus isolated from the bronchoalveolar lavage fluid of a critically ill patient could be neutralized by sera from several patients. Notably, we confirmed that 2019-nCoV uses the same cell entry receptor-angiotensin converting enzyme II (ACE2)-as SARS-CoV.

The above contents are the collected information from Internet and public resources to offer to the people for the convenient reading and information disseminating and sharing.

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