Review Article
The COVID-19 pandemic and the potential treatment of the novel coronavirus SARS-CoV-2

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Abstract: Coronavirus SARS-CoV-2 is a novel coronavirus and the seventh that can infect human beings and result in severe and acute respiratory syndrome and deaths. Currently, the world is undergoing a global health emergency due to the SARS-CoV-2 pandemic. As of May 18, SARS-CoV-2 has spread to over two hundred countries and infected more than 4.8 million people, resulting in over 300,000 deaths since the first case of a novel pneumonia (COVID-19) patient was discovered in Wuhan, China at the end of December 2019. Currently, there are no effective and/or approved targeting drugs for it though various supportive therapy drugs such as small molecule drugs, vaccines, antibodies and even Chinese herb medicines have been used in the treatment of the first-line patients. However, certain drugs such as remdesivir and S416 are under clinical investigation and may become therapeutic drugs. In this article, we review and discuss SARS-CoV-2, its person-to-person transmission, genomics and proteomics, and the potential for drug development.

Keywords: SARS-CoV-2, coronavirus, genomics, proteomics, epidemiology, remdesivir, S416, outbreak

Introduction

In December 2019, an unidentified pneumonia patient was first discovered in Wuhan, China [1, 2]. Subsequently, a novel coronavirus was isolated from early pneumonia patients, and named SARS-CoV-2 by the World Health Organization (WHO) on February 11. By the end of February 2020, the majority of the patients were still located in China (**Figure 1A**). Unfortunately, by now more than 200 countries have reported confirmed cases. WHO declared the novel coronavirus pneumonia (COVID-19) as a global pandemic on March 11. According to incomplete statistics, as of May 18, more than 4.84 million cases were diagnosed globally and 317,391 cases had died, with the mortality rate approximated at 6.56% (**Figure 1B**). The main reason for the large number of deaths is that there is no specific drug for the treatment of the coronavirus.

Fortunately, the results of clinical phase III trials of remdesivir showed that compared with placebo, it can significantly reduce the mortality and shorten the recovery time in adults hospitalized with COVID-19 [3].

SARS-CoV-2 is an enveloped, positive-strand RNA virus, and is the largest RNA virus (with the genome of 27~31.5 kb in size) discovered so far and belongs to Nidovirales, Coronaviridae. The Coronaviridae subfamily has been divided into four genera named Alphacoronvirus (αCoV), Betacoronavirus (βCoV), Gammacoronavirus (γCoV) and Deltacoronavirus (δCoV) [4, 5]. SARS-CoV-2 is a βCoV [6].

In this review, we have systematically summarized the epidemiology, morphology, genomics, proteomics, and the present research development of drugs of SARS-CoV-2.

Epidemiological investigation and analysis of SARS-CoV-2

Infectious source

The main sources of infection of COVID-19 were patients. In addition, asymptomatic COVID-19
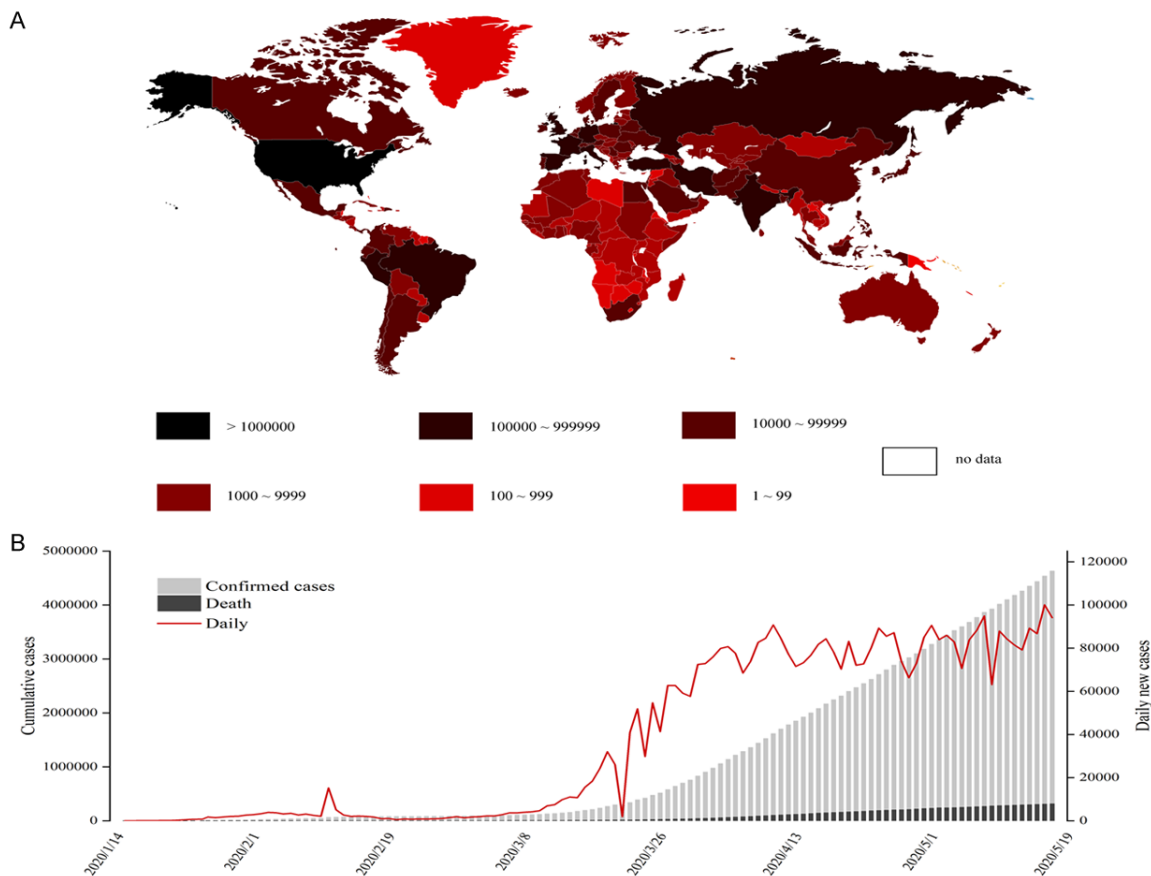
A

B

Figure 1. Statistical results of confirmed cases worldwide. A. Global distribution of confirmed cases. The shades of color represent different numbers of infected cases. The darker the color, the more confirmed cases. B. As of May 18, the number of confirmed cases in various countries around the world, after February 9 (not shown in **Figure 1**), the number of newly diagnosed cases in other countries in the world surpassed that of China, and this proportion has gradually increased since then.

carriers were also able to spread the virus. Some patients with asymptomatic infection have been detected with SARS-CoV-2 pathogenicity in their respiratory tracts [7]. Due to their physical characteristics, they do not show obvious clinical symptoms, but they can carry the virus themselves, and the virus can be transmitted to others [7]. Unlike patients, asymptomatic infections have no clinical symptoms and are difficult to detect in a timely manner. Therefore, if timely isolation and control measures cannot be taken for asymptomatic carriers, it may lead to a large number of leaks and transmission. Besides patients and asymptomatic infections, patients in the incubation period may also spread the virus. Together with the isolation and treatment of patients, the identification of asymptomatic infections must be a high priority.

To figure out the host of COVID-19, various methods such as deep learning algorithms were conducted. It was reported that SARS-CoV-2 was most closely related to bat-SL-CoVZC45 and bat-SL-CoVZXC21, with the similarity of 87.6% and 87.5% respectively [8]. SARS-CoV-2 was highly similar throughout the genome to Bat-CoV RaTG13 and the identity of whole genome sequence is 96.2% [9]. Based on the above results, some researchers predicted bats were the natural hosts of SARS-CoV-2 [8, 9]. It is generally believed that the intermediate host of SARS-CoV-2 would be wild animals, and humans are infected due to their close contact with these (killing and/or eating). Some scientists speculate that mink and pangolin may have been the intermediate hosts of this virus based on the mode of virus infection and multiple sequence alignments. However,

there is still no clear answer for the intermediate host of SARS-CoV-2 [10].

Transmission routes

The main routes of transmission of SARS-CoV-2 are droplet transmission and close contact transmission. These and other potential routes of COVID-19 transmission are discussed below.

I) Droplet transmission: The main transmission route of COVID-19, it is a respiratory disease that can easily spread to each other when sneezing or talking face to face; II) Intimate contact transmission: People can be infected by SARS-CoV-2 when they have direct physical contact with patients; III) Aerosol transmission: A densely populated and confined environment meets the conditions for aerosol transmission. These include confined space, extended time periods and high concentrations of virus in the air. Droplets mixed in the air form aerosols which cause infection after inhalation [11]. The risk of COVID-19 aerosol transmission can be effectively reduced by strengthening ventilation and environmental disinfection; IV) Fecal (urine)-oral transmission: There is no direct evidence that COVID-19 can be transmitted via the fecal (urine)-oral route. One Study have shown that 4 out of 62 stool samples (6.5%) were positive for Novel Coronavirus, and another 4 patients were positive for SARS-CoV-2 in the gastrointestinal tract, saliva, and urine. Another study showed positive results in oral swabs and fecal swabs by RT-PCR and serological test, indicating COVID-19 has the risk of fecal (urine)-oral transmission, and corresponding preventive work needs to be done; V) Mother-to-child transmission: A baby born to a COVID-19 patient was diagnosed with the virus only 30 h after his birth. This case indicates that SARS-CoV-2 may have a vertical transmission route from mother to child. Although the virus was positive in some patients' blood, the placental barrier would play an important role in avoiding virus infection to the baby, which means the concentration of COVID-19 has to be higher than a threshold [12]. Therefore, researchers estimated the transmission was still caused by contact.

Susceptible population

Among known cases, the youngest patient was a baby who was born just 30 h while the oldest patient was over 100 years old. Therefore, all age groups are susceptible to infection. It has been found that viral load and contact are two important factors for infection of COVID-19 [13]. The retrospective study indicated that the infection rate of medical staffs in Wuhan was 4.05%. Among medical workers, the infection rate has been seen as high as 29% (40/138). The number of infected males was statistically different in females. The data shows that men are more likely to be infected by COVID-19. Like SARS-CoV and MERS-CoV, SARS-CoV-2 infects human respiratory epithelial cells by S-protein interacting with human ACE2 [14, 15]. However, the expression of ACE2 in male cells is higher than that in female cells, which may lead to male infection more easily. The fatality rate was approximate 1.4% in the early stage of COVID-19 outbreak in China, which was lower than that of SARS and MERS. But the current fatality rates in several countries are over 7%.

Transmission dynamics

A study of about 425 cases showed 55% of the early cases (before Jan 1, 2020 - when the South China seafood Market was closed) were related to the market [16]. In subsequent cases of infection, the ratio decreased to 8.2%. The average incubation period of 425 patients involved in the study was 5.2 days (95% CI: 4.1-7.0). Every 7.4 days, the number of people infected with COVID-19 doubled. Recent epidemiological studies have reported that the average incubation period was shorter the previously indicated: 4.8 days (IQR: 3.0-7.2) [17]. Besides, 2.09% of the patients were medical stuffs, and only 1.18% of patients (13/1099) had a direct contact with wildlife. However, 31.30% had been to Wuhan and 71.80% had contact with people from Wuhan, indicating human-to-human transmission. 483 cases (43.95%) were local residents of Wuhan while 26.00% had not recently travelled to Wuhan or contacted with people from Wuhan.

The basic reproduction rate (R0) is another crucial parameter of COVID-19 that is not yet clear. In the early research, R0 was estimated based on the model of 425 cases' transmission and time fitting. According to the average continuous time interval of 7.5 days (95% CI: 5.3-19), R0 is inferred to be 2.2 (95% CI: 1.4-3.9) [16]. The WHO gave the estimation that the

R0 of COVID-19 is 1.4-2.5. In another study, groups from USA and UK. cooperated to determine R0. They assumed the incubation period of COVID-19 was 4.4 days which was similar to SARS. Based on the lift capacity of Wuhan, human-to-human transmission and diagnosed cases before Jan 22, 2020, they drew an epidemic model and estimated the R0 was approximate 3.1113. The authors ascribed the higher R0 to the use of data in the other province besides Hubei. Other researchers in Harvard University and Guangdong CDC gave their predicted R0, 2.0-3.1 and 2.9 respectively [18, 19]. A study based on the results of 5 independent models (Exponential growth, Maximum likelihood, Sequential Bayesian, Time-dependent reproduction numbers and SEIR) showed the R0 was 4.38 (95% CI: 3.63-5.13) before the city of Wuhan was administratively closed, 3.41 (95% CI: 3.16-3.65) after Wuhan closed and 3.39 (95% CI: 3.09-3.70) in the whole period [17]. With the development of the epidemic situation, another study used the chain binomial model to analyze the epidemiological data of 8866 patients. The results showed that R0 was 3.77 (95% CI: 3.51-4.05) based on the average incubation period of 5 days and the average continuous time interval of 7 days. It was higher than that of SARS (3.0) and MERS (< 1) [11].

Spread process

Since the first COVID-19 patient was discovered in December 2019, there were 4 stages in the COVID-19 transmission process: local outbreak, community transmission, wide transmission in China and worldwide transmission. The stage of local outbreak took place before Jan 1, 2020. The cases in this stage all linked to the South China Seafood Market. COVID-19 was exposed to more people around Wuhan and other provinces in the community transmission stage. The Spring Festival transportation caused frequent movement of population which led to wild and irresistible transmission of COVID-19 around China. Also contributing were parties and holidays during the Spring Festival, the lack of medical production, like surgical masks and disinfectant, which led to the dire consequences. The number of daily new cases increased dramatically during the whole of January. Fortunately, the Chinese government took strong and insightful measures such as the quarantine of Hubei province and the building of 14 module hospitals including Huoshenshan and Leishenshan hospitals. During this period, many countries provided their generous help. The effect of the struggle by the Chinese people and the help of other countries was obvious. The number of daily new cases decreased gradually following Feb 16, 2020 and the fatality rate was about 2.1% in China. On Feb 26, 2020, the number daily new cases in world other than China was 1027, which was the first day that China contributed less than 50%. The proportion of new cases in China continually decreased in the following days. On Mar 15, 2020, the number total cumulative cases were 153546, and the portion of China started to be less than half. China's portion decreased gradually in the following days, demonstrating the worldwide spread of COVID-19. Therefore, China will continue to face the serious risk of another outbreak due to case retransmission from outside the country.

The structure of SARS-CoV-2 under Cryo-EM

Like other coronavirus, particles of SARS-CoV-2 are moderately pleiomorphic or roughly spherical, with diameters of about 80-160 nm (**Figure 2**). The periphery is enveloped by lipid bilayers under Cryo-EM (**Figure 2A** green arrow), spike proteins of about 23 nm in whole length are embedded in the envelope (red arrow in **Figure 2A**), and the width of spike's head is approximately 7 nm (yellow arrow in **Figure 2A**), under the envelope is the nucleocapsid of the virus [20] (**Figure 2A** blue arrow). The structure of SARS-CoV-2 mode is shown in **Figure 2B**. It is vividly named as coronavirus because of its shape which is similar to the crown of medieval European kings.

Genomics and proteomics analysis of SARS-CoV-2

Genomics

The genome of SARS-CoV-2 is about 29.8 kb in size, with two flanking untranslated regions (UTR) and 14 open reading frames (ORFs) which encode 27 proteins. Located at the 5'-terminus of the genome, the orf1ab and orf1a genes encode the polyprotein pp1ab and pp1a respectively, which constitute 15 non-structural protein (nsps), including nsp1 to nsp16 apart from nsp11. Four structural proteins (M, N, E, and S) and eight accessory proteins (3a, 3b, 7a, 7b, 8b, 9b, p6, and orf14) are encoded at the 3'-terminus of the genome (**Figure 3**) [21].
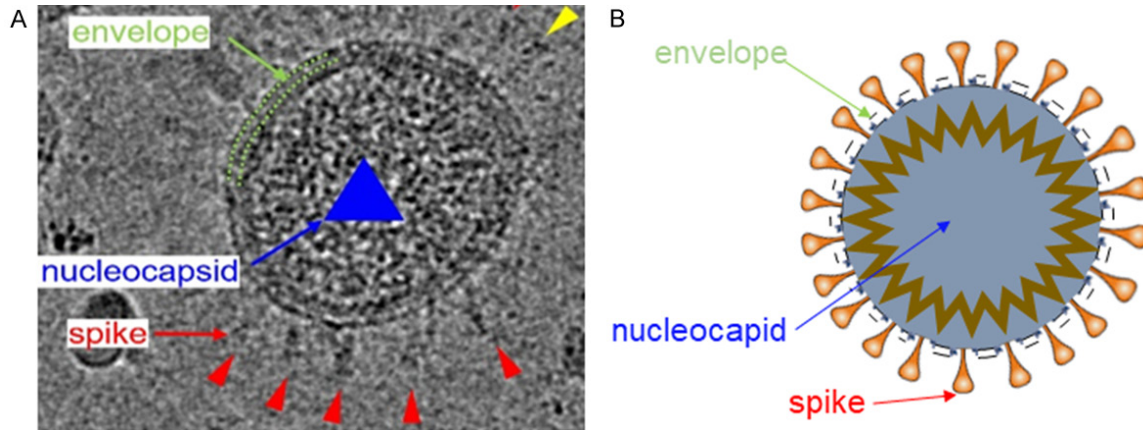
Figure 2. Morphology and mode structure of SARS-CoV-2 by Cryo-EM. A. Morphology of SARS-CoV-2 by Cryo-EM [20]. B. Mode structure of SARS-CoV-2.
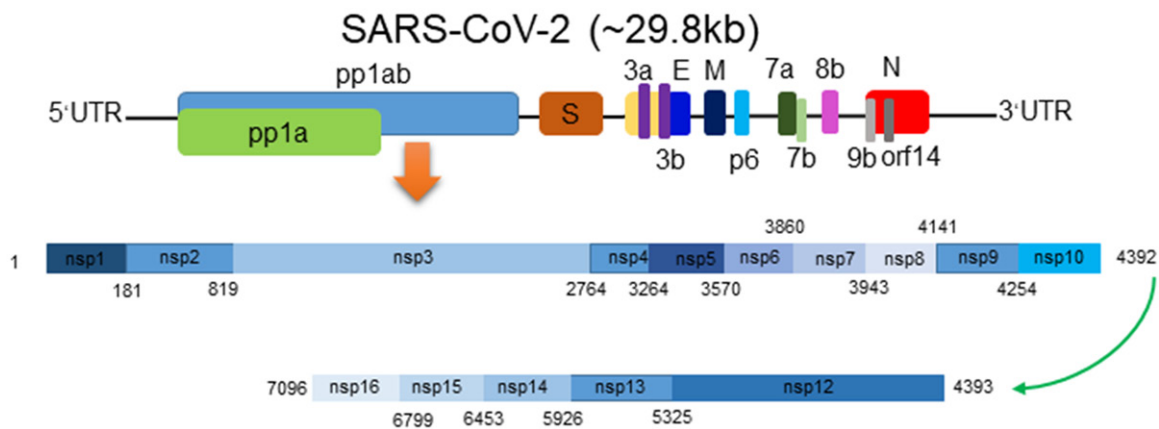

Figure 3. SARS-CoV-2 genome structure and its encoded proteins [21]. The genome of SARS-CoV-2 which is a positive-strand RNA virus encodes 15 non-structural proteins, 4 structural proteins, and 8 accessory proteins.

The results of genomic analysis showed that the sequence homology of SARS-CoV-2 and two other coronaviruses (bat-SL-CoVZC45 and bat-SL-CoVZXC21) collected in Zhoushan, Eastern China in 2018 was the highest, exceeding 87%. The sequence identities of SARS-CoV-2 in five gene regions (E, M, N, 7, 14) are more than 90%. The highest homology of E gene was 98.7%, and the lowest homology of S gene was only 75% [8]. The sequence identities of SARS-CoV-2 with the other two Coronavirus (SARS-CoV and MERS-CoV) were 79% and 50%, respectively [21].

Proteomics

Most of the coding proteins of SARS-CoV-2 are highly consistent with those of the bat-derived coronavirus. Most of the proteins encoded by SARS-CoV-2, bat-SL-CoVZC45 and bat-SL-CoV-ZXC21 have similar lengths, with few insertions or deletions [22]. The structural proteins of SARS-CoV-2 are the same as other coronaviruses, including spike (S) protein, envelope (E) protein, membrane (M) protein and nucleocapsid (N) protein. Among them, E, M and N proteins have more than 90% genetic similarity with SARS-CoV, but the S protein shows the largest difference at 76%. However, the protein structure of SARS-CoV-2 and MERS-CoV are quite different, the biggest similarity is in E protein, which is only 30%, and the similarities of M, N and S proteins are less than 10% [23].

It is worth noting that although SARS-CoV-2 is close to bat-SL-CoVZC45 and bat-SL-CoVZXC21 at the whole gene level, the external subdomain of its S protein receptor binding domain

Table 1. The drugs for SARS-CoV-2 in clinical research

Drugs	Targets	Ref.
Vaccines	S protein	[29]
Disulfiram	papain-like proteases	[26]
Thiopurine analogues	papain-like proteases	[33, 34]
Lopinavir	3C-like proteases	[35-38]
Ritonavir	3C-like proteases	[35-38]
ASC09F	3C-like proteases	-
Darunavir	3C-like proteases	[39]
Favipiravir	RdRp	[42]
Ribavirin	RdRp	[41]
Remdesivir	RdRp	[43, 44]
Arbidol	unknown	-
Oseltamivir	unknown	-
Corticosteroids	host	[16, 53]
Chloroquine	host	[44]
IFN-α2b	host	[35, 41, 51]
S416	host's DHODH	[48]
Tocilizumab	IL-6	[52]
Kevzara	IL-6	-

(RBD) is closer to SARS-CoV. Among the 14 amino acid sequences of S protein RBD in SARS-CoV, SARS-CoV-2 has 8 strictly conserved residues and 6 amino acid mutations, which may affect its selectivity and permeability.

Both SARS-CoV-2 and SARS-CoV enter host cells through the receptor angiotensin converting enzyme II (ACE2) [9, 24], and the cellular protease TMPRSS2 is used to activate the S protein. Whether the other two receptors of SARS-CoV (DC-SIGN and L-SIGN) are the receptors of SARS-CoV-2 has not been confirmed. Dipeptide peptidase 4 (DPP4), the main receptor of MERS-CoV, however, has been proved not to be the receptor of SARS-CoV-2.

At the amino acid level, SARS-CoV-2 and SARS-CoV are also similar, but there are still some differences. For example, the 8a protein is not existent in SARS-CoV-2; the 8b protein has 84 amino acids in SARS-CoV, but 121 amino acids in SARS-CoV-2; the 3b protein has only 22 amino acids in SARS-CoV-2, but 154 amino acids in SARS-CoV [21]. The orf8 protein of SARS-CoV-2 does not contain any known functional domain or motif, while an aggregation motif VLVVL (75-79 amino acids) was found in orf8b of SARS-CoV, which can activate NLRP3 inflammasome in macrophages [25].

Progress in drug research of SARS-CoV-2

The COVID-19 is a sudden-onset infectious disease. Unfortunately, there are still no effective drugs for treating it. As our own professional experience confirms, it is a long process from research and development to broad availability of an innovative drug, so the fastest path is to screen out potentially effective therapeutic drugs including vaccines from already approved listed drugs (**Table 1**).

At present, drug targets for SARS-CoV-2 are mainly divided into two categories: one approach targets viral proteins, such as spike protein, papain like protease, 3C like protease, RNA dependent RNA polymerase, while other approaches are based on host targeting [26, 27].

Development for different types of SARS-CoV-2 vaccines

Currently, more than 70 kinds of SARS-CoV-2 vaccines under development worldwide contains live-attenuated vaccines, subunit vaccines, mRNA vaccines, DNA vaccines, live-vector vaccines and peptide vaccines, some of them have entered clinical trials [28]. For instance, one adenovirus type-5 (Ad5) vectored COVID-19 vaccine expressing S protein now has been in clinical phase III trials, because the vaccine showed good tolerance in clinical phase I trials, and produced immune response to SARS-CoV-2 in humans [29]. Unfortunately, however, another vaccine from Oxford University have already failed, six vaccinated monkeys were infected with SARS-CoV-2 once again, although antibodies were produced.

A problem in vaccine development is that SARS-CoV-2 only induces mild disease in transgenic animals expressing human ACE2, while wild-type mice cannot be infected, so it is difficult to establish an animal model of SARS-CoV-2 vaccine for the toxic tests. Besides, the S protein of SARS-CoV-2 not only plays an important role in receptor binding but also exhibits other biological activity which may cause severe liver damage and leads to antibody-dependent enhancement (ADE). To fight the coronavirus pandemic which has occurred every decade in 21th century, an effective vaccine may be needed [30].
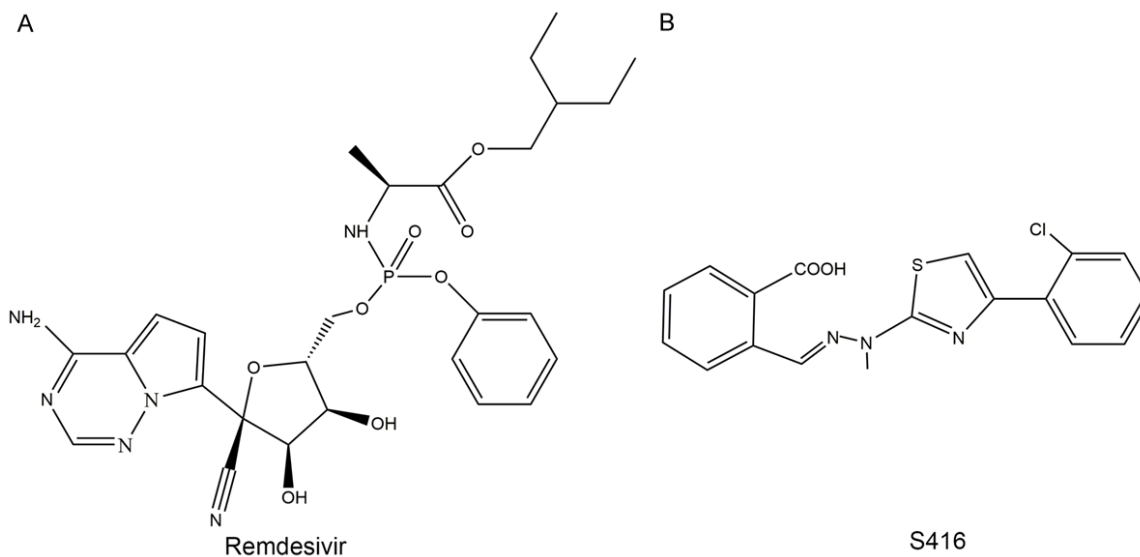
Figure 4. Small molecule compounds Remdesivir and S416. Remdesivir targets viral RNA-dependent RNA polymerase (A), S416 targets the host's DHODH (B) [48], both of them have broad-spectrum antiviral activities.

Viral S protein

Coronaviruses enter the cell by the spike (S) protein binding to the receptor ACE2, but the S proteins need to be cleaved before they can function. It is found that SARS-CoV-2 has a new Furin Protease cleavage site, so the development of Furin protease inhibitor is of great significance for the treatment of COVID-19 [31, 32]. But unfortunately, no drug for this target is currently entering clinical trials.

Non-structural proteins of SARS-CoV-2

The non-structural proteins of coronavirus are significant for its. At present, the main drugs targeting non-structural proteins are disulfiram, lopinavir, ritonavir, asc09f, darunavir, favipiravir, ribavirin, penciclovir, remdesivir, galidesivir, and S416 [26].

Disulfiram is a drug approved for the treatment of alcoholism. It has been shown that disulfiram can effectively inhibit the papain-like proteases activity of MERS-CoV and SARS-CoV [26]. In addition, drugs targeting papain-like proteases also include thiopurine analogues [33, 34]. However, SARS-CoV-2-related drugs currently being developed for this target are mainly focused on pre-clinical research.

Targets for drugs such as lopinavir, ritonavir, ASC09F, and darunavir are 3C-like proteases. These drugs affect viral replication by targeting 3C-like proteases [35-38]. Lopinavir, ritonavir and darunavir have been approved for HIV treatment [39]. ASC09F for HIV is in clinical research. Unfortunately, recent research by academician Wang Chen et al. showed that lopinavir and ritonavir, which have previously entered clinical phase III, were not effective in treating severe patients of COVID-19. The results have been published in NEJM [40]. Deliravir and ASC09F are still in clinical phase III trials of COVID-19.

The target of drugs such as fapilavir, ribavirin, penciclovir, redecvir, and galidivir is RNA-dependent RNA polymerase (RdRp). These drugs are nucleoside analogs that block viral RNA synthesis by targeting RdRp, and ultimately inhibit viral replication. Fapilavir, ribavirin, and penciclovir were approved for the treatment of influenza, hepatitis C virus (HCV)/respiratory syncytial virus (RSV), and herpes simplex virus (HSV), respectively [41, 42]. At present, only papavivir and ribavirin are conducting clinical research on COVID-19. Galidivir was originally developed for the treatment of HCV but preclinical studies have shown excellent antiviral activity against SARS-CoV-2 [26, 43, 44].

Previously, a patient with SARS-CoV-2 infection in the United States recovered under the treatment of remdesivir, so it has attracted considerable attention. Remdesivir (**Figure 4A**), also known as GS-5734, is the monophosphoramide prodrug of GC-441524, which is a C-adeno-

sine nucleoside analogue. Studies show that remdesivir targets RNA-dependent RNA polymerase and therefore has broad-spectrum antiviral activity against Ebola-Kikwit, Ebola-Makona, Sudan virus, Bundibugyo virus, Marburg virus, MERS-CoV in vitro (EC_{50} = 0.02 µM-10 µM) [45]. In Vero E6 cells, the EC_{50} of SARS-CoV-2 = 1.76 µM [44].

There are also drugs that target SARS-CoV-2, but whose targets are unknown. Examples include arbidol and oseltamivir, both of which are used for the treatment of influenza. Abidol inhibits influenza infection by binding influenza virus's hemagglutinin to affect its membrane fusion with host cells. Oseltamivir is a neuraminidase inhibitor that affects virus-infected cells by inhibiting the neuraminidase activities of the influenza viruses. Neither of these drug targets exists in the SARS-CoV-2. Although the mechanism against the novel coronavirus is still unclear, these two drugs both have significant effects in the treatment of COVID-19, and phase IV clinical studies of patients have been conducted [26, 46, 47].

Targeting human related proteins

Recently, Rui Xiong reported that a small molecule compound named S416 (**Figure 4B**) inhibited SARS-CoV-2 more effectively than remdesivir, with EC_{50} = 17 nM in Vero E6 cells, much less than 1.76 µM. But the target of S416 is inconsistent with that of remdesivir. It targets the host's DHODH, a rate-limiting enzyme in pyrimidine synthesis in vivo, which blocks viral RNA replication by efficiently inhibiting pyrimidine synthesis, but has low toxicity to cells. It is currently effective against influenza viruses (EC_{50} = 0.01-0.06 µM), SARS-CoV, MERS-CoV, Ebola (EC_{50} = 0.018 µM), Zika virus (EC_{50} = 0.021 µM) and circulating SARS-CoV-2 [48].

At the same time, a series of clinical symptoms such as inflammatory response and cytokine storm have been reported in patients infected with SARS-CoV-2. Corticosteroids, Chloroquine, Interferon α2b (IFN-α2b), Tocilizumab, and Kevzara have entered the clinical research. Corticosteroids are mainly used in anti-inflammatory therapy, and studies have shown that they have therapeutic effects on the clinical response caused by SARS-CoV-2 [49, 50]. Chloroquine is mainly used in anti-malarial and autoimmune diseases, and recent studies have shown that it has a broad spectrum of antiviral effects, mainly by regulating the pH in the body

to affect viral infections [27, 44]. IFN-α2b is an immunomodulator that produces antiviral effects by improving the immunity of patients [35, 36, 51]. Tocilizumab is the first approved IL-6 blocking antibody that specifically binds membrane IL-6 receptors and soluble IL-6 receptors and inhibits signal transduction. It has been proven safe in the treatment of rheumatoid arthritis [52]. In the United States and European Union, tocilizumab has also been approved to treat severe and life-threatening cytokine release syndrome (CRS) associated with chimeric antigen receptor T cell (CAR-T) therapy. Clinical studies have shown that patients with COVID-19 had a rapid decrease in fever within days after receiving tocilizumab, and 75% of patients (15 of 20) had reduced need for supplemental oxygen. Based on these results, China has recently updated the COVID-19 treatment guidelines and approved the use of tolicizumab as an antibody drug to treat critically ill patients. Similar to tocilizumab, Kevzara is a fully human monoclonal antibody that targets the IL-6 receptor. Sanofi and its partner Regeneron will jointly conduct clinical trials. Regeneron will lead clinical trials in the United States while Sanofi will lead clinical trials outside the United States, including in areas such as Italy that are more affected by COVID-19.

Conclusion

The worldwide pandemic of COVID-19 has caused, and will further cause immeasurable losses to the global economy. Effective medical interventions are in urgent needs. Whether it is remdesivir, reported at the beginning of the epidemic, or S416, which has recently been reported to be more effective, we hope that these two new drugs will achieve good clinical efficacy and bring the epidemic to an end as soon as possible. Another exciting news is that on March 20, 2020, the Angus Cameron team by analyzing global data, found that the higher the outdoor ambient temperature, the lower the incidence of COVID-19! So far, we human beings have never been overwhelmed by a pandemic, nor we will be this time, but we must learn from it. For instance, strengthening the international medical communities to defeat this new challenge.

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