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Review on structural mechanism and mode of action of corona virus

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ABSTRACT

Human coronaviruses, first reported in the 1960s, were the reason for a large number of children infected with the upper respiratory tract. SARS and four other coronaviruses have been reported since 2003, causing substantial morbidity and mortality. A new coronavirus was firstly reported from Hubei Province, Wuhan City in China, in December 2019 and named as novel Corona Virus. Later on, this virus is referred to as COVID-19, which can cause diseases similar to SARS and named for the spikes that protrude from their membranes, like the sun's corona. The virus is believed to have been spread by animals sold in Wuhan from the seafood market and Health authorities in China reported fever, cough, breathing problems, and pneumonia in patients. The virus has a variety of physical and pathogenic features similar to the SARS-CoV-2 virus. Closer contact may cause the virus to be transmitted Initial flu-like symptoms, such as fever, cough, myalgia, and dyspnea in the 2-14 days of viral contact. People who are chronically ill are usually older or have medical co-morbidity. No treatments or virus vaccines are currently available. Seasonal Influenza has less mortality rate and less infectious than SARS-CoV-2. Many of the viruses remain to be identified as they will spread. Future directions for SARS-CoV work include greater knowledge of the replication process, tropism, and immune-response mechanisms, taking account of the possible functions of groups-specific proteins; development of animal and human virus vaccine strategies, and anti-viral therapies and very likely isolation and characterization of new human pathogenic coronaviruses. Emergencies for identifying and quarantining contaminated individuals early in the process of preventing their further spread are being made through global efforts.

Keywords: Virus, corona, pathogen, disease, human, SARC, respiratory.

INTRODUCTION: Coronaviruses (CoVs) are of the Coronaviridae family. All Coronaviruses are characteristically pleomorphic RNA viruses that contain crown-shaped peplomers of 80-160 nM and are of the positive polarity of 27-32 kb (Woo *et al.*, 2010). The envelope includes usually three different proteins for the virus: S, M, and E (Lu, 2020). Coronaviruses are primarily attributed to the observation of MERS-CoV and Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) in their physical and chemical characteristics. Coronaviruses are sensitive to UV and heat and can effectively be inactivated after 30 minutes of heating at 56 °C and lipid solvents such as ether, chlorine-containing disinfectant, 75% ethanol, chloroform, and peroxyacetic acid except for chlorhexidine (Jin *et al.*, 2020). Recombined coV levels are very high because of continuous (RdRP) jumps and transcription errors. Coronaviruses are zoonotic pathogens with a higher mutation rate, in both species humans and animals with a wide range of clinical features, from asymptomatic to intensive care needs, which contribute to infections within humans 'digestive, gastrointestinal, hepatic, and neurological systems (Sahin *et al.*, 2020). It was not considered particularly human-pathogenic until they were found for the first time in 2002 and 2003, in Guangdong State of China with the severe acute respiratory syndrome (SARS). There were two more prevalent forms of CoV before these outbreaks, such as OC43 and 229E CoV, which caused more mild infections in those with an adequate immune system (Baseer *et al.*, 2016). The extremely pathogenic CoV, (MERS-CoV) know as Middle East Respiratory Syndrome Coronavirus was detected this time nearly ten years after SARS (Imai *et al.*, 2020). A common cold, pneumonia (pneumonia), and severe acute respiratory syndrome (SARS) is associated with this infection and can affect humans and animals. These are common in animals around the world, but few are known to influence human beings. Inadequate infection prevention procedures in healthcare facilities have been established from records of morbidity and death of health workers infected with MERS-CoV. This prompted Health Minister to highlight the need for stringent complexity in healthcare facilities by sensitizing healthcare staff to the guidance on infection management recommended by the Disease Control Center (CDC) and (WHO). These recommendations protected normal safeguards, droplets, airborne and eye protection in case of suspicious or contaminated MERS-CoV cases (Memish *et al.*, 2014).

The latest KSA research reveals strong comprehension and a constructive outlook towards MERS. The two most well-known CoV types, CoV OC43, and CoV 229E were more likely to cause mild infection in those with an appropriate immune system before these outbreaks (Yin and Wunderink, 2018). Another public health issue that becomes the focus of global attention, arises in December 2019 from Coronavirus in the state of Wuhan where livestock farming is also traded (Wang *et al.*, 2015). On 12 December 2019 unexplained case of pneumonia was identified and probable influenza and other coronaviruses have been ruled out by laboratory studies. The new Coronavirus type (novel Coronavirus) was announced by Chinese authorities on 7 January 2020 (Lu, 2020). On 11 February 2020, the WHO (World Health Organization) called

this virus COVID-19. As of 12 February 2020, a total of 43,103 cases were registered with 1,018 deaths (McIntosh *et al.*, 2020). An increased number of cases in Wuhan City results in the second transmission of human to human cases following market closure and case evacuation in China (Sahin *et al.*, 2020). The most frequent symptom included fever of 98.6 percent, exhaustion of 69.6%, dry cough (59.4%), yalgia (34.8 %), and dyspnea of 31.2 % in the largest case series reported by JAMA (Lu, 2020). The median patient aged 56 years was infected with the disease. Vingt-six percent of the patients have been admitted to the ICU. The average age admits to the ICU was usually 66 years old and most had other medical conditions. At present, the COVID-19 result was not strengthened by antibiotic or antiviral evidence. Researchers started investigating the coronavirus origins immediately (Sahin *et al.*, 2020). Before symptoms begin, the virus can be transmitted which was another concern. The time of incubation from symptom presentation is 2 to 14 days (Imai *et al.*, 2020). This virus spread rapidly across China and worldwide throughout the new year in China (12 February 2020) within one month. When there are high rates of human mobility and the unite among Chinese and millions, this outbreak was extended into 13 towns, including the Hubei Province, where holidays are being kept and travel restrictions relaxed (Rothe *et al.*, 2020; Ullah, 2020). As of 25 January 2020, 42 deaths have been recorded in the present outbreak and some 1400 people have been infected in China, Japan, the United States, South Korea, Thailand, Vietnam, Taiwan, and Singapore. There is no clear evidence yet of SARS-CoV-2 vaccination, a Canadian company claiming to have produced and launched human vaccines in summer 2021 (Lai *et al.*, 2020). The number of Severe Acute Respiratory Syndrome Coronavirus known as SARS-CoV-2 cases is expected to continue to increase in the next months. To diagnose the virus, treat for the disease, and prevention of spread, an early indication of flu-like signs in a patient with recent journeying to China or access to those infected with the virus is important. Much research on the source of SARS-CoV-2, its diagnosis, mode of transmission, and successful vaccine. Having responded quickly to this new virus, the scientific community has already published several articles on this outbreak. In March 2020 we reviewed all the latest coronavirus articles published (Adhikari *et al.*, 2020; Nishiura, 2020). The purpose of this study is to summarize and critically analyze the structure, transmission, and mode of action of the early findings process of the coronavirus. This study can provide valuable information on the topic for future research and can contribute both domestically and internationally.

History of coronavirus: Human coronaviruses started to occur in 1965 when a virus named B813 was detected in Tyrrell and Bynoe (Tyrrell *et al.*, 1975). Human fetal tracheal organ cultures acquired by an adult with a common cold in the respiratory system have been observed. Infectious agent presence was shown by inoculation in human volunteers, the medium deriving from these cultures. In the majority of subjects, colds were produced but Bynoe and Tyrrell and at that point, we're unable to develop the agent in tissue culture. At about the same time, Hamre and Procknow (Hamre and Procknow, 1966) could grow an unusual tissue culture virus, from samples collected from students of medical with cold. Both Hamre and B814 virus she named 229E, are susceptible to others and thus a lipid-containing coat is probably required for infectivity, but those two viruses have not had any contact with any known myxo-or paramyxo viruses. Scientists documented the recuperation of different strains of ether-sensitive agents of the respiratory tract of humans by the use of techniques close to those of Tyrrell and Bynoe during their research at the laboratory of Robert Chanock. These viruses have been named "OC" to indicate that they are produced in organ cultures. Almeida and Tyrrell applied electron microscopy on B814-infected organ cultures fluids during the same timeframe and found particles identical to the viral chickens' bronchitis virus; Pleomorphic, membrane-coating, and mostly coated with scattered club-shaped surface projections the medium size (80–150 nm) particles. Hamre and Procknow identified the 229E agent and studied previous OC viruses had a similar structure (Wu *et al.*, 2020).

In the 1960s Tyrrell headed a virologists' unit working with several animal viruses and human strains. This contained infectious bronchitis viruses, hepatitis mouse viruses, and others which were all morphologically similar to those seen in electron microscopy. The new virus group was later recognized as a new genus officially and was named coronavirus, which refers to the surface projection's crown appearance (Tyrrell *et al.*, 1975). A great deal of expertise was acquired from continuing serological research on the human respiratory coronaviruses epidemiology. Airborne coronavirus infections have been shown to occur more frequently in winter and spring in temperate climates than in summer and fall. In the three decades following their detection of human strains OC43 and 229E, primarily due to the simplest working conditions, were researched. OC43 showed that the mouse hepatitis virus is closely connected and was modified for the development of subsequent tissue culture and suckling mouse brain. Strain 229E is cultured from clinical samples directly in tissue culture. The 2 viruses displayed regularity, with major epidemics emerging at periods of two to three years (Zhang *et al.*, 2019). Strain 229E is typically an epidemic in the US, although strain OC43 is more vulnerable to scattered outbreaks. Infection can occur at any age, but in children, it was most common. Given the broad emphasis on strains 229E and OC43 alone, it became clear that there are other strains of coronavirus too. Paraskevis *et al.* (2020) reveals that either OC43 or 229E was not comparable in serology with the coronavirus strain B814. They found that 3 out of the 6 strains mentioned previously were only marginally related to OC43 or 229E because of different strain variations in the coronavirus family.

Animal coronaviruses have been increasingly numerous and important, while work was ongoing to study the epidemiology and pathogenicity of human coronaviruses. Coronaviruses, identified earlier, caused disease in several species of animals including rabbits, rats, turkeys, mice, chickens, calves, chickens, dogs, pigs, and cats (Zhu *et al.*, 2020; Ontiveros *et al.*, 2003; Nishiura *et al.*, 2020; Zhu *et al.*, 2020). The antigenic and genetic components in animal and human coronaviruses have been divided into 3 broad groups. Group I had 229E virus and other viruses, group II had OC43 virus, and Group III had air bronchitis virus and a variety of other avian viruses. Group II included virus OC43.

CoV genome and structure: Coronaviruses in electron micrographs are RNA viruses and the diameter is around 120

nm of medium size 80-160 nM crown-shaped peplomers and 27-32 kb positive polarity (Woo *et al.*, 2010) with a very distinctive appearance. The 30 kb long nucleic acid is positive, polyadenylated, and single-stranded. RNA is the most widely recognized RNA and it codes for a large polyprotein (Zhu *et al.*, 2020). This polyprotein is divided by viral-encoded proteases, which are: ATPase helicase and RNA-dependent RNA polymerase; a protein called surface hemagglutinin-esterase which is available on OC43 (Human coronavirus OC43) and many other groups two coronaviruses; the petal-shaped surface projections which is formed by the large surface glycoprotein (S protein) and the complex with the RNA is formed by M protein known as membrane glycoprotein; a tiny envelope protein (E protein); and a nucleo-capsid protein (N protein) (Zhu *et al.*, 2020) as shown in figure 1. The coding functions of many other ORFs (open reading frames) are not clear. The coronavirus replication strategy consists of a nested collection of RNAs with common polyadenylated 3-end. Only the unique 5-end is translated. Mutations in nature are common. Coronaviruses may also recombine genetically if 2 viruses simultaneously invade the same cell.

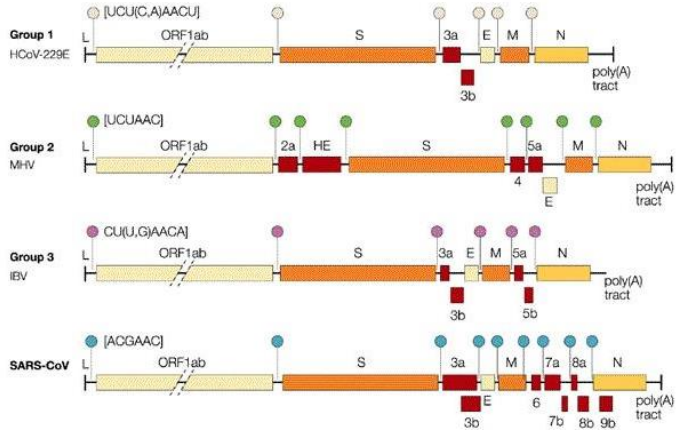

Figure 1: Figure 1: Comparison of genome structures of coronavirus (Wrapp *et al.*, 2020)

Virion proteins: Three big structural protein coronaviruses have integral membrane glycoprotein which is small (M, E 1) a nucleocapsid protein (N), and a large spike glycoprotein (S, E2) as shown in figure 2. Although these proteins are present in all coronavirus, a subset (HEV, HCV-OC43, and BCV) is now identified to have an additional glycopolypeptide (gp65), which is not related to S or M (Wrapp *et al.*, 2020).

Nucleocapsid protein (N): Amino acids count in N protein and JHM, IBV strains of Beaudette, cloned and sequenced for MHV A59 strains, and M41 for TGEV and BCV (Corman *et al.*, 2020). These proteins are fundamental, the fundamental residues in clusters; the C terminus is acidic. 8 to 10 ~ of the total amino acids are the serine residues; the fact that N is phosphorylated on serines, in particular, may be related to their clustering. The BCV N protein homology with MHV is 70 ~ (72 ~ base homology), of TGEV 29 (37 ~ base homology), and IBV 29 ~o (43 9/0 base homology. A prominent homological area consists of approximately 68 amino acids which display a similarity of 51 to 79 ~ depending on the pairs of virus compared (Paraskevis *et al.*, 2020).

Membrane glycoprotein (M): As with the N-protein, M-glycoprotein also exhibits different values known as Mr in polyacrylamide gels in the different coronaviruses. All coronaviruses grow within the infected cell cytoplasm, budding from the endoplasmic reticulum to the cytoplasmic vesicles. Such vesicles are extruded, released, or Expelled in the same time frame from the cell (Xu *et al.*, 2020). A different group of coronaviruses uses different enzymes and others as its cellular receptor. The SARS coronavirus for its cellular receptor uses angiotensin-converting enzyme II (Li *et al.*, 2005).

Spike glycoprotein (S): Spike protein S1: Link the virion with the host receptor to the cell membrane, starting the infection (By similarity). The incorporation into human CLEC4M/DC-SIGNR and ACE2 receptors and the internalization of the virus into host cell endosomes cause S-glycoprotein configuration changes. Cathepsin CTSL proteolysis can unmask the S2 fusion peptide and cause membrane fusion in endosomes (Xu *et al.*, 2020).

Spike protein S2: Mediates virion fusion and cell membranes as a viral fusion protein of class I. The protein in the known model has a total of three conformational states, post-fusion hairpin state, pre-hairpin intermediate state, and pre-fusion native state. The coil areas (heptad repeats) assume a trimmer-of-hairpin structure during viral and target cell membrane fusion, placing the fusion peptide near the region called C-terminal of the ectodomain. The creation of this structure tends to Result in viral and target cell membranes apposition and subsequent fusion (Li *et al.*, 2005; Xu *et al.*, 2020).

Spike protein S2': Acts like a peptide of viral fusion which unmasked the following S2 cleavage as shown in figure 3; occurs upon endocytosis of the virus.

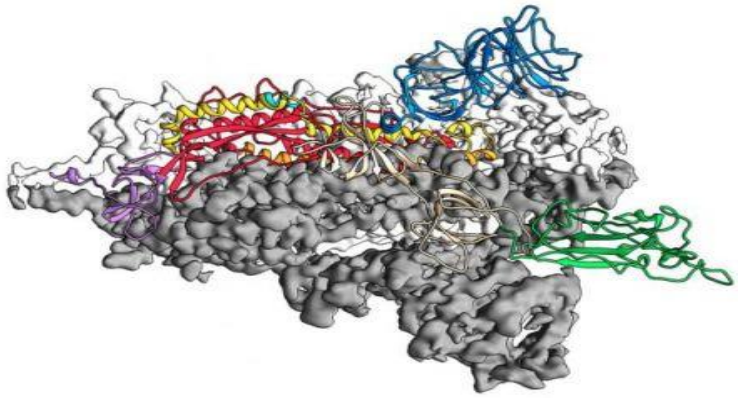

Figure 2: Figure 2: Side view on the spike protein of the SARS-CoV-2 in colored ribbons with one receptor-binding domain (Wrapp *et al.*, 2020).

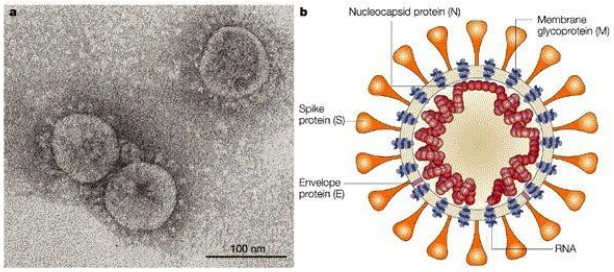

Figure 3: Figure 3: SARS coronavirus anatomy.

Structural similarities with other groups: Coronavirus is a Pathogen enveloped containing 27 to 32 kb of single-stranded RNA (Cui *et al.*, 2019). CoV is now the largest recorded virus with RNA Extreme acute respiratory syndrome outbreak known as SARS-CoV in 2003 and Mild Eastern Respiratory

Syndrome-CoV (MERS-CoV) in 2012 had become more common over the last 20 years in the science and medical communities. Each genus tends to infect a certain host form. Before the new epidemic, six COVs are blamed for infection of humans, the worst is the MERS-CoV and SARS-CoV and four others are triggering moderate respiratory symptoms, both high and low. Beta-coronaviruses, like SARS-CoV, MERS-CoV, and now SARSCoV-2, target mammals while birds are affected by delta-coronavirus. Bats are considered the largest beta-coronavirus reservoirs; other mammals, like dromedary camels for MERS-CoV and palm civets for SARS-CoV, act as intermediate hosts. A CoV becomes a zoonotic virus when the disease has been introduced into humans, as recorded in all three CoV outbreaks (Song *et al.*, 2019).

SARS-CoV-2 shares similarities with SARS-CoV, such as physical structure and pathogenic behavior. CoVs use a protein known as the Spike protein (S) for binding to target cells. The overall sequence comparisons between the SARS-CoV-spike and 2019 nCoV-spike are about 76% –78% for the whole protein, about 73% –76% for the RBD (Receptor Binding Domain) which contains the critical neutralizing domain (CND) which can induce extremely potent antibody neutralization and cross-protection against divergent SARS-CoV strains which can help in the production of vaccines and 50% to 53% for the RBM [Receptor Binding Motive] which binds to a claw-like structure's surface of ACE2 which helps in the recognition of the structure. Although there are numerous similarities between SARS-CoV-2 and the SARS-CoV, Two other coronaviruses are closest to SARS-CoV-2, which suggest that bats are the virus reservoir (Hoffmann *et al.*, 2020; Xu *et al.*, 2020).

Transmission of COVID-19: Human coronaviruses are frequently transmitted through the air from an infected to another person; by sneezing and coughing. Close physical contact like a handshake and rubbing or touching your nose, eyes, and face after rubbing an item with hand on the surface with a virus as shown in figure 4 (Hoffmann *et al.*, 2020). In the US, human beings are normally affected by common coronavirus. Most individuals become infected throughout their lives with one or more common human coronaviruses. Small children would be affected most likely. However, people may have multiple infections during their lives (Syed, 2020).

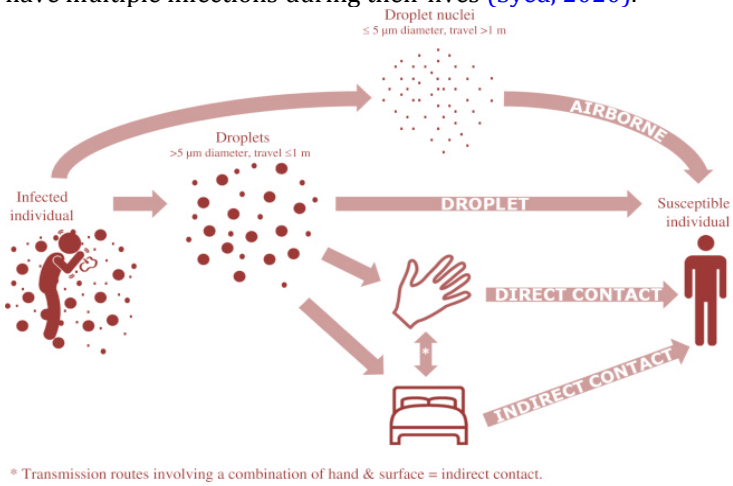

Figure 4: The potential role of dry surfactants in healthcare is to spread SARS and MERS coronaviruses and influenza viruses (Otter *et al.*, 2016).

Particles of coronavirus have spiked proteins stippled out from their surfaces, and they connect these spikes to the cell membranes, which allow the genetic material of the virus to enter human cells and continues to "hijack the cell metabolism that lets the virus replicate, and then" crawls slowly down the bronchial tubes". Once the virus enters the lungs, the mucous membranes of the lungs are inflamed. It can hurt alveoli or lung bags, which can also appear to be rectal. Thus, although the virus tends to be zero in the lungs, it may even be able to penetrate the gastrointestinal system cells, experts claim. That may explain why certain patients have signs such as diarrhea or indigestion. The virus can also get into the bloodstream (Lauer *et al.*, 2020).

Incubation period: The COVID-19 requires a host for its survival and the hosts maybe humans and animals for their replication. They can live for up to 72 hours on non-soft surfaces like plastic and steel and cardboard for up to 24 hours but only around four hours this virus remained viable on copper. So, washing hands after touching the surfaces decrease the chances for it to spreading. To estimate the incubation time for COVID-19, there were 181 confirmed cases of clearly visible exposure and initiation times. The median period of incubation recorded was 5.1 days (95% CI, 4.5% to 5.8 days) and is 9 7.5% within 11.5 days (8.2 to 15.6 days) of the person developing symptoms. Figures indicate that 101 out of 1000s cases (99th percentile, 482), after 14 days of intensive surveillance or quarantine would have symptoms as shown in figure 5 (Lauer *et al.*, 2020).

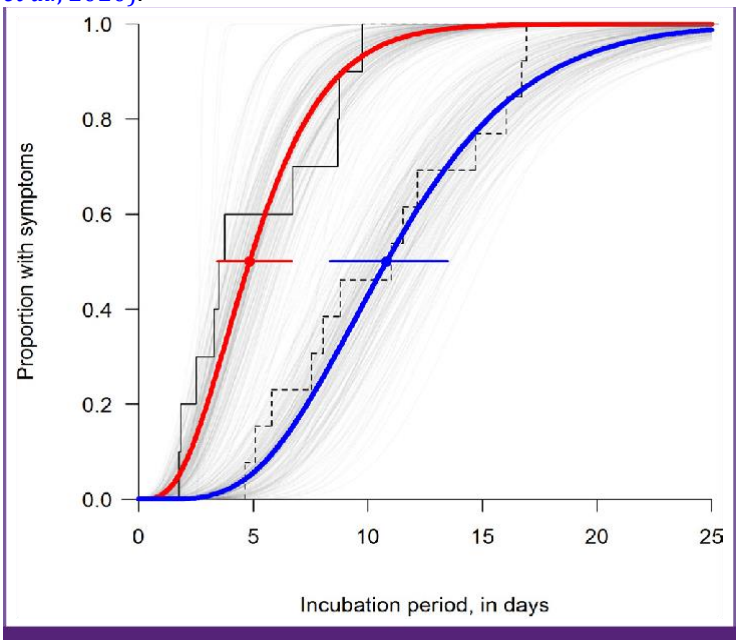

Figure 5: Distribution of incubation periods in two Daejeon hospitals for cases of Middle East respiratory syndrome-coronavirus infection. Hospital A (blue line) and B (red line) fitted incubation time distribution is compared to the cumulative empirical density function of observations (average duration of the onset of the symptoms) (black line). (Blackline) The 95 percent intervals of confidence are also reported for the media of these fitted distributions. In gray shad-ing bootstrap, estimates are shown (Park *et al.*, 2016).

Disease symptoms: Different coronaviruses such as NL63, 229E, OC43, and in the upper respiratory tract, HKU1 usually causes mild to moderate diseases such as a common cold. Many

people are infected with these viruses at a different point in their lives. Such diseases typically only survive for a brief period. Symptoms usually include a flowy nose, a general feeling of being unwell, headache, cough, fever, and sore throat. Human coronaviruses also cause disorders in the lower respiratory tract, such as pneumonia and bronchitis. It is most commonly found in individuals with heart disease, compromised immune systems, babies, and older adults. Sometimes severe signs have occurred in two additional coronaviruses, the MERS-CoV and the SARS-CoV (Lai *et al.*, 2020). MERS signs usually include fever, cough, and breathlessness that often contribute to pneumonia. For every 10 MERS registered, approximately 3 or 4 patients have died. SARS also included fever, chills, and body aches that typically developed into pneumonia. Since 2004, no human SARS cases in the world have been registered (Ghinai *et al.*, 2020).

CONCLUSION: The creation of SARS and the detection of coronavirus as a causative agent of the infections like respiratory, gastrointestinal, hepatic, and neurologic systems was a surprise to the coronavirus community, as it was the first conclusive association of coronavirus with serious disease in humans. Although it is not clear if SARS-CoV will re-emerge in the human population, it has generated awareness to recognize coronaviruses as the source of human respiratory and probably other forms of the disease. Data collected over the long years of animal coronavirus research also allowed for very fast identification of SARS-CoV and genome sequence. The knowledge that multi-gene viral pathogenesis and in particular the kind of immune response are contributing indicates that minor sequence changes can have significant effects on the pathogenic phenotype. Experiences with coronavirus vaccine production can also lead to the development of SARS vaccines. Future directions for SARS-CoV work include greater knowledge of the replication process, tropism, and immune-response mechanisms, taking account of the possible functions of groups-specific proteins; development of animal and human virus vaccine strategies, and anti-viral therapies and very likely isolation and characterization of new human pathogenic coronaviruses. Our experience of other coronaviruses is likely to speed up the understanding of SARS-CoV, as summarized above.

CONFLICT OF INTEREST: Authors have no conflict of interest.

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