IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Human Journals
Review Article
July 2022 Vol.:24, Issue:4

Coronavirus (COVID-19): Introduction, Virion Structure, and Biological Properties

IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Shivanshu Sharma

Assistant Professor, Sharda University, Greater Noida, India.

Submitted: 24 June 2022
Accepted: 29 June 2022
Published: 30 July 2022

Keywords: Coronavirus, Middle East respiratory syndrome (MERS), severe acute respiratory syndrome (SARS)

ABSTRACT

COVID-19 is one of the global pandemic situation in the world that affect in every corner of the world including territorial, political, ideological, religious, cultural, and certainly academic boundaries. Coronaviruses (CoVs), enveloped positive-sense RNA viruses, are characterized by club-like spikes that project from their surface, an unusually large RNA genome, and a unique replication strategy. Coronaviruses cause a variety of diseases in mammals and birds ranging from enteritis in cows and pigs and upper respiratory disease in chickens to potentially lethal human respiratory infections. The rapid spread of the coronavirus disease 2019 (COVID-19), caused by a zoonotic beta-coronavirus entitled 2019 novel coronavirus (2019-nCoV), has become a global threat. This virus was reported to be a member of the b group of coronaviruses. The novel virus was named as Wuhan coronavirus or 2019 novel coronavirus (2019-nCoV) by the Chinese researchers.

INTRODUCTION

Coronavirus derived from the Latin *corona* meaning "*Crown*" or "*halo*" which refers to characteristics of appearance reminiscent of a crown or a solar corona around the virions (virus particles) when viewed under 2-D Transmission Electron Microscope (TEM), due to the surface covering in club-shaped protein spikes.

Coronaviruses which are directly relate to ***Coronaviridae*** family in the ***Nidovirales*** order. Corona, crown-like spikes, outer surface of the virus and so called coronavirus.

COVID-19, respiratory disease caused by a novel(SARS-CoV-2), evolved into a global pandemic.[1]Public health and healthcare professionals are at the frontline, working to contain and to mitigate the spread of this disease.

Remarkably rapid progress has been made in biological and biomedical research, including identifying the virus, sequencing its genes, and resolving cogent protein structures. The manufacture of testing and diagnosis kits and development and trials of vaccines, antiviral drugs, and other medical and psychological interventions are also being accelerated. Although these activities may seem a bit far from the fields of physical sciences and engineering that typically work with inanimate objects, and should be done to help in such a global crisis. To start, one would need to establish basic understanding of the infection pathways of respiratory diseases and the virion (i.e., viable virus) structure.

CORONAVIRUS (COVID-19)

Coronavirus disease 2019(COVID-19) is an emerging disease with a rapid increase in cases and deaths since its first identification in Wuhan, China, in December 2019. Limited data are available about coronavirus disease 2019 during pregnancy; however, information on illnesses associated with other highly pathogenic coronaviruses (ie, SARS and the MERS) might provide insights into coronavirus disease 2019's effects during pregnancy.[1] Coronaviruses cause illness ranging in severity from the common cold to severe respiratory illness and death. Currently, the primary epidemiologic risk factors for coronavirus disease 2019 include travel from mainland China (especially Hubei Province) or close contact with infected individuals within 14 days of symptom onset.[2] Data suggest an incubation period of 5 days (2 to14 days). The average age of hospitalized patients has been 49 to 56 years, with a third to half with an underlying illness. Children have been rarely reported. Men were more frequent among hospitalized cases (54-73%). Frequent manifestations include fever, cough,

myalgia, headache, and diarrhea. Abnormal testing includes abnormalities on chest radiographic imaging, lymphopenia, leukopenia, and thrombocytopenia. Initial reports suggest that acute respiratory distress syndrome develops in 17 to 29% of hospitalized patients. Overall case fatality rate appears to below 1%; however, early data may overestimate this rate. In 2 reports describing 18 pregnancies with coronavirus disease 2019, all were infected in the third trimester, and clinical findings were similar to those in non-pregnant adults. Fetal distress and preterm delivery were seen in some cases. But 2 pregnancies were cesarean deliveries and no evidence of in utero transmission was seen. Data on SARS and MERS in pregnancy are sparse. For SARS, the largest series of 12 pregnancies had a case-fatality rate of 25%. Complications included acute respiratory distress syndrome in 4, disseminated intravascular coagulopathy in 3, renal failure in 3, and secondary bacterial pneumonia in 2, and sepsis in 2 patients. Mechanical ventilation was 3 times more likely among pregnant compared with nonpregnant women. Among 7 first-trimester infections, 4 ended in spontaneous abortion. Four of 5 women with SARS after 24 weeks gestation delivered preterm. For MERS, there were 13 case reports in pregnant women, of which 2 were asymptomatic, identified as part of a contact investigation; 3 patients (23%) died. Two pregnancies ended in fetal demise and 2 were born preterm. No evidence of in utero transmission was seen in SARS or MERS. Currently, no coronavirus-specific treatments have been approved by the US Food and Drug Administration. Because coronavirus disease 2019 might increase the risk of pregnancy complications, management should optimally be in a health care facility with close maternal and fetal monitoring. Principles of management of coronavirus disease 2019 in pregnancy include early isolation, aggressive infection control procedures, oxygen therapy, avoidance of fluid overload, consideration of empiric antibiotics (secondary to bacterial infection risk), laboratory testing for the virus and coinfection, fetal and uterine contraction monitoring, early mechanical ventilation for progressive respiratory failure, individualized delivery planning, and a team-based approach with multispecialty consultations.

VIRION STRUCTURE

Coronavirus virions are spherical with diameters of approximately 125 nm as depicted in recent studies by cryo-electron tomography and cryo-electron microscopy [2,3]. The most prominent feature of coronaviruses is the club-shaped spike projections emanating from the surface of the virion. These spikes are a defining feature of the virion and give them the appearance of a solar corona, prompting the name, coronaviruses. Within the envelope of the

virion is the nucleocapsid. Coronaviruses have helically symmetrical nucleocapsids, which is uncommon among positive-sense RNA viruses, but far more common for negative-sense RNA viruses.

Coronavirus virus particles contain four main structural proteins. These are the spike (S), membrane (M), envelope (E), and nucleocapsid (N) proteins, all of which are encoded within the 3′ ends of the viral genome. The S protein (~150 kDa), utilizes an N-terminal signal sequence to gain access to the ER and is heavily N-linked glycosylated. Homotrimers of the virus-encoded S protein make up the distinctive spike structure on the surface of the virus [4,5]. The trimeric S glycoprotein is a class I fusion protein [6] and mediates attachment to the host receptor [7]. In most, but not all, coronaviruses, S is cleaved by a host cell furin-like protease into two separate polypeptides noted as S1 and S2 [8,9]. S1 makes up the large receptor-binding domain of the S protein while S2 forms the stalk of the spike molecule [10].

The M protein is the most abundant structural protein in the virion. It is a small (~25–30 kDa) protein with 3 transmembrane domains [11] and is thought to give the virion its shape. It has a small N-terminal glycosylated ectodomain and a much larger C-terminal endodomain that extends 6–8 nm into the viral particle [12]. Despite being co-translationally inserted in the ER membrane, most M proteins do not contain a signal sequence. Recent studies suggest the M protein exists as a dimer in the virion and may adopt two different conformations allowing it to promote membrane curvature as well as bind to the nucleocapsid [13].

The E protein (~8–12 kDa) is found in small quantities within the virion. E proteins from coronaviruses are highly divergent but have a common architecture [14]. The membrane topology of E protein is not completely resolved but most data suggest that it is a transmembrane protein. The E protein has an N-terminal ectodomain and a C-terminal endodomain and has ion channel activity. As opposed to other structural proteins, recombinant viruses lacking the E protein are not always lethal although this is virus type dependent [15]. The E protein facilitates assembly and release of the virus (see the section on Assembly and Release of Coronaviruses), but also has other functions. For instance, the ion channel activity in SARS-CoV E protein is not required for viral replication but is required for pathogenesis [16].

The N protein constitutes the only protein present in the nucleocapsid. It is composed of two separate domains, an N-terminal domain (NTD) and a C-terminal domain (CTD), both capable of binding RNA *in vitro*, but each domain uses different mechanisms to bind RNA. It

has been suggested that optimal RNA binding requires contributions from both domains [17, 18]. N protein is also heavily phosphorylated [19], and phosphorylation has been suggested to trigger a structural change enhancing the affinity for viral versus non-viral RNA. N protein binds the viral genome in a beads-on-a-string type conformation. Two specific RNA substrates have been identified for N protein; the TRSs [20] and the genomic packaging signal [21]. The genomic packaging signal has been found to bind specifically to the second, or C-terminal RNA binding domain [22]. N protein also binds nsp3 [18,23], a key component of the replicase complex, and the M protein[24]. These protein interactions likely help tether the viral genome to the replicase-transcriptase complex (RTC) and subsequently package the encapsidated genome into viral particles.

A fifth structural protein, the hemagglutinin-esterase (HE), is present in a subset of β-coronaviruses. The protein acts as a hemagglutinin, binds sialic acids on surface glycoproteins, and contains acetyl-esterase activity [25]. These activities are thought to enhance S protein-mediated cell entry and virus spread through the mucosa [26]. Interestingly, HE enhances murine hepatitis virus (MHV) neurovirulence [27]; however, it is selected against in tissue culture for unknown reasons [28].

PATIENT WORKFLOW

Administration (FDA) approved therapeutics or vaccines for the treatment of COVID-19 patients.[29,30]Diagnostics can playan important role in the containment of COVID-19, enabling the rapid implementation of control measures that limit the spread through case identification, isolation, and contact tracing (i.e.,identifying people that may have come in contact with an infected patient). The current diagnostic workflow forCOVID-19 is described in Figure 1.

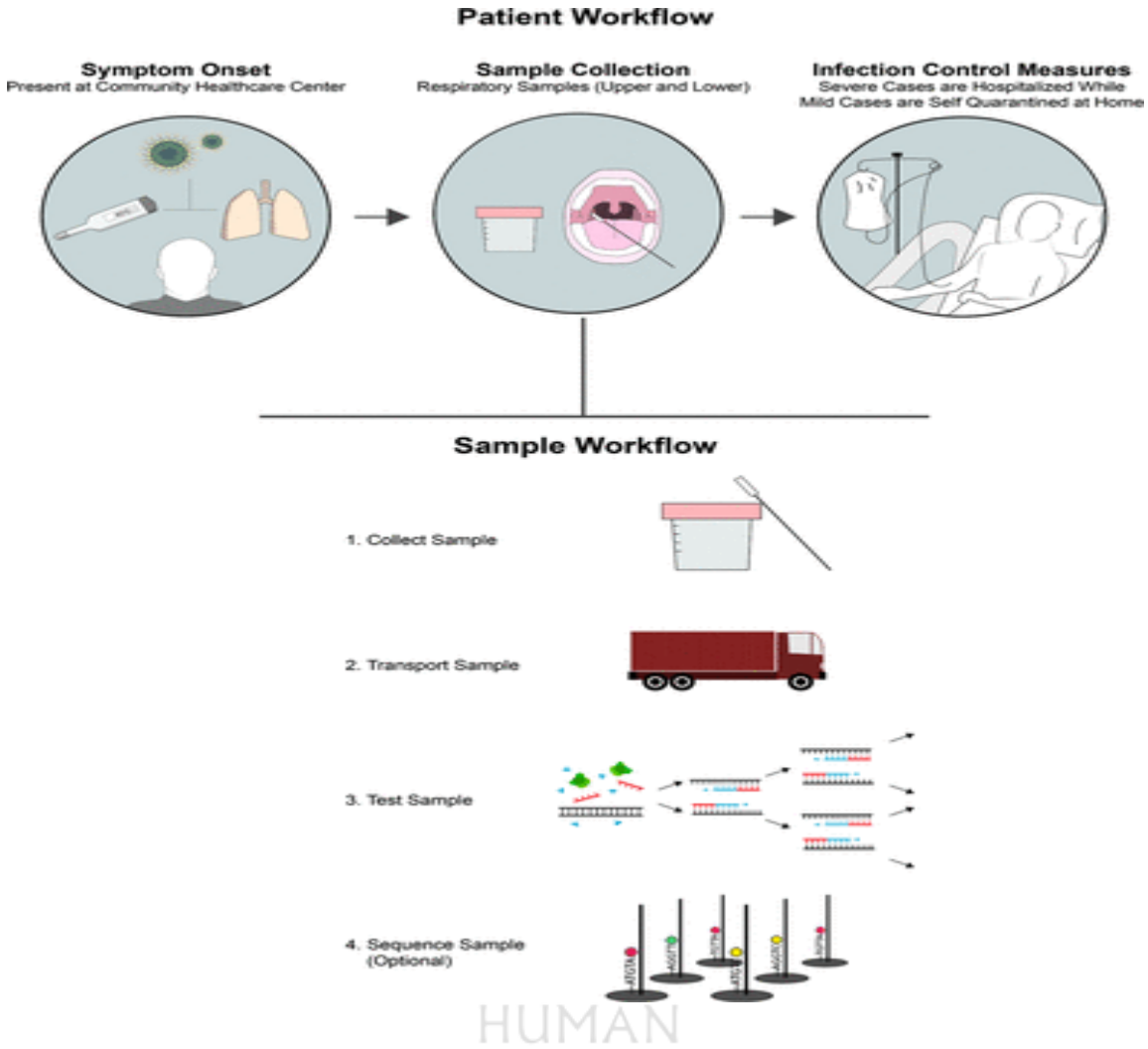

Figure No. 1. Example of patient and sample workflow during the COVID-19 outbreak. Patients present at a healthcare facility for triage. The collected samples are tested on-site if possible or transported for molecular testing and sequencing. Patients have then managed appropriately.

Biological Properties of SARS-CoV-2.

SARS-CoV-2 was first identified from patient samples in Wuhan, China. Human airway epithelial cells were cultured with the virus from BAL fluid isolated from patients. Supernatant was collected from cells that were damaged or killed and analyzed by negatively stained transmission electron microscopy (Figure 2).[31]The images revealed that the virus has a diameter ranging from 60to 140 nm, has an envelope with protein spikes, and has genetic material.[32]The overall structure looks similar to other viruses belonging- to the *Coronaviridae* family.SARS-CoV-2 has a single-stranded positive sense RNA genome that is 30,000 nucleotides in length.[1,33]The genome encodes 27 proteins including an RNA-dependent RNA Biological Properties of SARS-CoV-2. SARS-CoV-2 was first identified

from patient samples in Wuhan, China. Human airway epithelial cells were cultured with the virus from BAL fluid isolated from patients. The supernatant was collected from cells that were damaged or killed and analyzed by negative stained transmission electron microscopy (Figure 2).[31] The images revealed that the virus has a diameter ranging from 60to 140 nm, has an envelope with protein spikes, and has genetic material.[32]The overall structure looks similar to other viruses from the Coronaviridae family.SARS-CoV-2 has a single-stranded positive sense RNA genome that is 30,000 nucleotides in length.[1,33]The genome encodes 27 proteins including an RNA-dependent RNA polymerase (RdRP) and four structural proteins.[33,34] RdRP acts in conjunction with nonstructural proteins to maintain genome fidelity. A region of the RdRP gene in SARS-CoV-2 was shown to be highly similar to a region of the RdRP gene found in batcoronavirus RaTG13 and 96% similar to the RaTG13 overall genome sequence. Of 104 strains sequenced between December 2019 and mid-February 2020, 99.9% sequence homology was observed, but, more recently, changes in the viral genome have been catalogued, showing a higher sequence diversity.[2,35]

The four structural proteins of SARS-CoV-2 include the spike surface glycoprotein (S), small envelope protein (E), matrix protein (M), and nucleocapsid protein (N). In coronaviruses, the S gene codes for the receptor-binding spike protein that enables the virus to infect cells.[36] This spike protein mediates receptor binding and membrane fusion, which determines host tropism and transmission capabilities. In SARS-CoV-2, the S gene is divergent with <75% nucleotide sequence similarity when compared to all previously described SARS-related coronaviruses. The other three structural proteins are more conserved than the spike protein and are necessary for general coronavirus function.[33]These proteins are involved in encasing the RNA and/or in protein assembly, budding, envelope formation, and pathogenesis.[37-39]

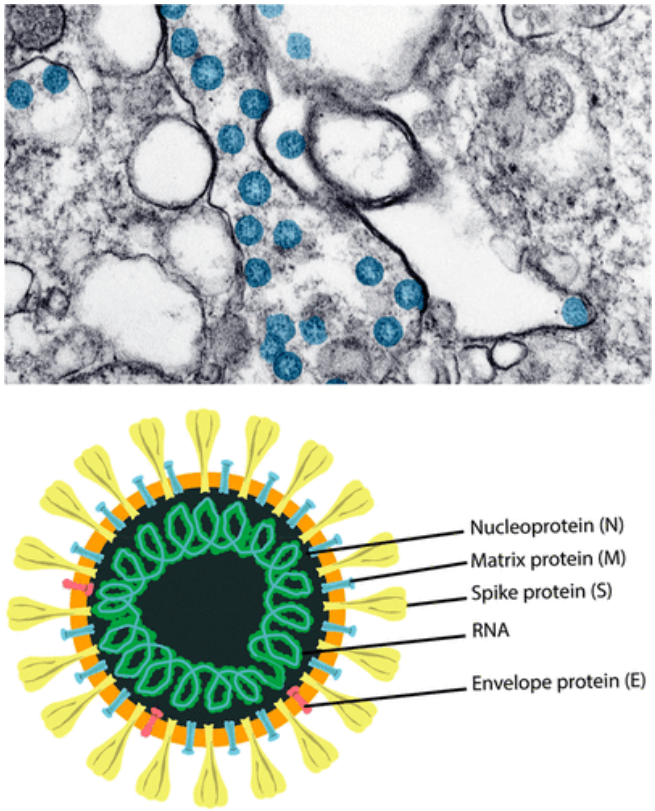

Figure No. 2. SARS-CoV-2 morphology. Transmission electron microscope image of SARS-CoV-2 spherical viral particles in a cell. The virus is colorized in blue (adapted from the US Centers for Disease Control). Representation of the viral structure is illustrated with its structural viral proteins.

CONCLUSION

In this article describes the introduction, biological properties, Virolgy and virion structure of coronavirus (nCoV) disease which are currently emerged from Wuhan, China in December 2019. **Coronavirus disease 2019(COVID-19)** is an emerging disease with a rapid increase in cases and deaths since its first identification in Wuhan, China, in December 2019. Limited data are available about coronavirus disease 2019 during pregnancy; however, information on illnesses associated with other highly pathogenic coronaviruses (ie, SARS and the MERS) might provide insights into coronavirus disease 2019's effects during pregnancy. Apart from the other viruses, COVID-19 may cause rare side effects to those patients, after some time of the treatment.

REFERENCES

1. https://pubs.acs.org/doi/10.1021/acsnano.0c02618
2. Barcena M, Oostergetel GT, Bartelink W, Faas FG, Verkleij A, Rottier PJ, Koster AJ, Bosch BJ. Cryo-electron tomography of mouse hepatitis virus: Insights into the structure of the coronavirion. Proceedings of the National Academy of Sciences of the United States of America. 2009; 106(2):582–587. [PubMed: 19124777]
3. Neuman BW, Adair BD, Yoshioka C, Quispe JD, Orca G, Kuhn P, Milligan RA, Yeager M, Buchmeier MJ. Supramolecular architecture of SARS coronavirus revealed by electron cryomicroscopy. Journal of virology. 2006; 80(16):7918–7928. [PubMed: 16873249]
4. Beniac DR, Andonov A, Grudeski E, Booth TF. Architecture of the SARS coronavirus prefusion spike. Nature structural & molecular biology. 2006; 13(8):751–752.
5. Delmas B, Laude H. Assembly of coronavirus spike protein into trimers and its role in epitope expression. Journal of virology. 1990; 64(11):5367–5375. [PubMed: 2170676]
6. Bosch BJ, van der Zee R, de Haan CA, Rottier PJ. The coronavirus spike protein is a class I virus fusion protein: structural and functional characterization of the fusion core complex. J Virol. 2003; 77(16):8801–8811. [PubMed: 12885899]
7. Collins AR, Knobler RL, Powell H, Buchmeier MJ. Monoclonal antibodies to murine hepatitis virus-4 (strain JHM) define the viral glycoprotein responsible for attachment and cell--cell fusion. Virology. 1982; 119(2):358–371. [PubMed: 6281979]
8. Abraham S, Kienzle TE, Lapps W, Brian DA. Deduced sequence of the bovine coronavirus spike protein and identification of the internal proteolytic cleavage site. Virology. 1990; 176(1):296–301. [PubMed: 2184576]
9. Luytjes W, Sturman LS, Bredenbeek PJ, Charite J, van der Zeijst BA, Horzinek MC, Spaan WJ. Primary structure of the glycoprotein E2 of coronavirus MHV-A59 and identification of the trypsin cleavage site. Virology. 1987; 161(2):479–487. [PubMed: 2825419]
10. de Groot RJ, Luytjes W, Horzinek MC, van der Zeijst BA, Spaan WJ, Lenstra JA. Evidence for a coiled-coil structure in the spike proteins of coronaviruses. J Mol Biol. 1987; 196(4):963–966. [PubMed: 3681988]
11. Armstrong J, Niemann H, Smeekens S, Rottier P, Warren G. Sequence and topology of a model intracellular membrane protein, E1 glycoprotein, from a coronavirus. Nature. 1984; 308(5961):751–752. [PubMed: 6325918]
12. Nal B, Chan C, Kien F, Siu L, Tse J, Chu K, Kam J, Staropoli I, Crescenzo-Chaigne B, Escriou N, van der Werf S, Yuen KY, Altmeyer R. Differential maturation and subcellular localization of SARS coronavirus surface proteins S, M and E. The Journal of general virology. 2005; 86(Pt 5):1423–1434. [PubMed: 15831954]
13. Neuman BW, Kiss G, Kunding AH, Bhella D, Baksh MF, Connelly S, Droese B, Klaus JP, Makino S, Sawicki SG, Siddell SG, Stamou DG, Wilson IA, Kuhn P, Buchmeier MJ. A structural analysis of M protein in coronavirus assembly and morphology. Journal of structural biology. 2011; 174(1):11–22. [PubMed: 21130884]
14. Godet M, L'Haridon R, Vautherot JF, Laude H. TGEV corona virus ORF4 encodes a membrane protein that is incorporated into virions. Virology. 1992; 188(2):666–675. [PubMed: 1316677]
15. DeDiego ML, Alvarez E, Almazan F, Rejas MT, Lamirande E, Roberts A, Shieh WJ, Zaki SR, Subbarao K, Enjuanes L. A SARS coronavirus that lacks the E gene is attenuated in vitro and in vivo. Journal of virology. 2007; 81(4):1701–1713. [PubMed: 17108030]
16. Nieto-Torres JL, Dediego ML, Verdia-Baguena C, Jimenez-Guardeno JM, Regla-Nava JA, Fernandez-Delgado R, Castano-Rodriguez C, Alcaraz A, Torres J, Aguilella VM, Enjuanes L. SARS coronavirus envelope protein ion channel activity promotes virus fitness and pathogenesis. PLoS pathogens. 2014; 10(5):1004077.
17. Chang CK, Sue SC, Yu TH, Hsieh CM, Tsai CK, Chiang YC, Lee SJ, Hsiao HH, Wu WJ, Chang WL, Lin CH, Huang TH. Modular organization of SARS coronavirus nucleocapsid protein. Journal of biomedical science. 2006; 13(1):59–72. [PubMed: 16228284]
18. Hurst KR, Koetzner CA, Masters PS. Identification of in vivo-interacting domains of the murine coronavirus nucleocapsid protein. Journal of virology. 2009; 83(14):7221–7234. [PubMed: 19420077]
19. Stohlman SA, Lai MM. Phosphoproteins of murine hepatitis viruses. Journal of virology. 1979; 32(2):672–675. [PubMed: 228084]
20. Stohlman SA, Baric RS, Nelson GN, Soe LH, Welter LM, Deans RJ. Specific interaction between coronavirus leader RNA and nucleocapsid protein. Journal of virology. 1988; 62(11):4288–4295. [PubMed: 2845141]

21. Molenkamp R, Spaan WJ. Identification of a specific interaction between the coronavirus mouse hepatitis virus A59 nucleocapsid protein and packaging signal. Virology. 1997; 239(1):78–86. [PubMed: 9426448]
22. Kuo L, Masters PS. Functional analysis of the murine coronavirus genomic RNA packaging signal. Journal of virology. 2013; 87(9):5182–5192. [PubMed: 23449786]
23. Hurst KR, Koetzner CA, Masters PS. Characterization of a critical interaction between the coronavirus nucleocapsid protein and nonstructural protein 3 of the viral replicase-transcriptase complex. Journal of virology. 2013; 87(16):9159–9172. [PubMed: 23760243]
24. Sturman LS, Holmes KV, Behnke J. Isolation of coronavirus envelope glycoproteins and interaction with the viral nucleocapsid. Journal of virology. 1980; 33(1):449–462. [PubMed: 6245243]
25. Klausegger A, Strobl B, Regl G, Kaser A, Luytjes W, Vlasak R. Identification of a coronavirus hemagglutinin-esterase with a substrate specificity different from those of influenza C virus and bovine coronavirus. Journal of virology. 1999; 73(5):3737–3743. [PubMed: 10196267]
26. Cornelissen LA, Wierda CM, van der Meer FJ, Herrewegh AA, Horzinek MC, Egberink HF, de Groot RJ. Hemagglutinin-esterase, a novel structural protein of torovirus. Journal of virology. 1997; 71(7):5277–5286. [PubMed: 9188596]
27. Kazi L, Lissenberg A, Watson R, de Groot RJ, Weiss SR. Expression of hemagglutinin esterase protein from recombinant mouse hepatitis virus enhances neurovirulence. Journal of virology. 2005; 79(24):15064–15073. [PubMed: 16306577]
28. Lissenberg A, Vrolijk MM, van Vliet AL, Langereis MA, de Groot-Mijnes JD, Rottier PJ, de Groot RJ, et al. Luxury at a cost? Recombinant mouse hepatitis viruses expressing the accessory hemagglutinin esterase protein display reduced fitness in vitro. Journal of virology. 2005; 79(24):15054–15063. [PubMed: 16306576]
(29) Coronavirus Disease 2019 (COVID-19); U.S. Food and DrugAdministration. http://www.fda.gov/emergency-preparedness-andresponse/mcm-issues/coronavirus-disease-2019-covid-19 (accessed2020/03/03).
(30) Liu, C.; Zhou, Q.; Li, Y.; Garner, L. V.; Watkins, S. P.; Carter,L. J.; Smoot, J.; Gregg, A. C.; Daniels, A. D.; Jervey, S.; et al. Researchand Development on Therapeutic Agents and Vaccines for COVID-19 and Related Human Coronavirus Diseases. ACS Cent. Sci. 2020, 6, 315−331.
(31) Details on COVID-19; Public Health Image Library (PHIL),Centers for Disease Control and Prevention. https://phil.cdc.gov/Details.aspx?pid=23354 (accessed 2020/03/27).
(32) Zhu, N.; Zhang, D.; Wang, W.; Li, X.; Yang, B.; Song, J.; Zhao,X.; Huang, B.; Shi, W.; Lu, R.; et al. A Novel Coronavirus fromPatients with Pneumonia in China, 2019. N. Engl. J. Med. 2020, 382(8), 727−733.
(33) Wu, A.; Peng, Y.; Huang, B.; Ding, X.; Wang, X.; Niu, P.; Meng,J.; Zhu, Z.; Zhang, Z.; Wang, J. Commentary Genome Compositionand Divergence of the Novel Coronavirus (2019-nCoV) Originatingin China. Cell Host Microbe 2020, 27, 325.
(34) Sexton, N. R.; Smith, E. C.; Blanc, H.; Vignuzzi, M.; Peersen,O. B.; Denison, M. R. Homology-Based Identification of a Mutationin the Coronavirus RNA-Dependent RNA Polymerase That ConfersResistance to Multiple Mutagens. J. Virol. 2016, 90 (16), 7415−7428.
(35) Tang, X.; Wu, C.; Li, X.; Song, Y.; Yao, X.; Wu, X.; Duan, Y.;Zhang, H.; Wang, Y.; Qian, Z.; et al. On the Origin and ContinuingEvolution of SARS-CoV-2. National Science Review 2020,DOI: 10.1093/nsr/nwaa036.
(36) Wrapp, D.; Wang, N.; Corbett, K. S.; Goldsmith, J. A.; Hsieh,C.-L.; Abiona, O.; Graham, B. S.; McLellan, J. S. Cryo-EM Structureof the 2019-nCoV Spike in the Prefusion Conformation. Science 2020,367, 1260.
(37) Lim, Y.; Ng, Y.; Tam, J.; Liu, D. Human Coronaviruses: AReview of Virus−Host Interactions. Diseases 2016, 4 (4), 26.
(38) Neuman, B. W.; Kiss, G.; Kunding, A. H.; Bhella, D.; Baksh, M.F.; Connelly, S.; Droese, B.; Klaus, J. P.; Makino, S.; Sawicki, S. G.;et al. A Structural Analysis of M Protein in Coronavirus Assembly andMorphology. J. Struct. Biol. 2011, 174 (1), 11−22.
(39) Schoeman, D.; Fielding, B. C. Coronavirus Envelope Protein:Current Knowledge. Virol. J. 2019, 16 (1), 69.