Global Scientific JOURNALS

GSJ: Volume 12, Issue 9, September 2024, Online: ISSN 2320-9186
www.globalscientificjournal.com

DIFFERENCES BETWEEN COVID-19 AND OTHER CORONAVIRUSES.

ABSTRACT.

COVID-19, the disease caused by SARS-CoV-2, is a highly contagious disease.. Its clinical characteristics were very similar to those of viral pneumonia. After analysis of respiratory samples from infected patients, the experts at the People Republic of China (PRC) Centers for Disease Control declared that the pneumonia-like infection, later known as novel coronavirus pneumonia (NCP), was caused by a novel coronavirus (Huang C *et al*, 2020). The World Health Organization (WHO) officially named the disease 'COVID-19'. The International Committee on Taxonomy of Viruses named the virus 'severe acute respiratory syndrome coronavirus 2' (SARS-CoV-2). Assigning a formal name for the novel coronavirus and the disease it causes is neccesary to identify the virus in clinical, medical and scientific research.This article is therefore aimed at providing clarity on "why covid-19 is different from other coronaviruses?"

INTRODUCTION.

Coronaviruses are a group of enveloped viruses with non-segmented, single-stranded, and positive-sense RNA genomes. Coronaviruses can infect animals and also humans, causing respiratory, gastrointestinal, hepatic, and neurological infections (Weiss and Leibowitz, 2011). As the largest known RNA viruses, Coronaviruses are further divided into four classes: alpha-coronavirus, beta- corona□virus, gamma-coronavirus and delta-coronavirus (Yang and Leibowitz, 2015).

Apart from infecting different variety of vertebrates such as chicken, pigs and bat, six coronaviruses have been known to infect human hosts and cause respiratory diseases. They include...

1. 229E (alpha coronavirus)

2. NL63 (alpha coronavirus)

3. OC43 (beta coronavirus)
4. HKU1 (beta coronavirus)

5. MERS-CoV (beta coronavirus)

6. SARS-CoV (beta coronavirus) (Drosten *et al,* 2020).

Among them, Severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) are zoonotic and highly contagious coronaviruses that have resulted in regional and global pandemics. Coronaviruses possess a distinctive morphology, the name being derived from the outer fringe of embedded envelope protein. Members of the family Coronaviridae cause a broad spectrum of animal and human infections. Human coronavirus (HCoV) infection causes respiratory diseases with mild to severe outcomes. In the last decade, the world have witnessed the emergence of two zoonotic infections, highly pathogenic Human coronaviruses: severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV). Replication of Human coronavirus is regulated by a diversity of host factors and induce draconian alterations in cellular structure and physiology.

Coronaviruses make up a large family of viruses that can infect birds and mammals, including humans, according to world health organisation (WHO). These viruses have been responsible for several outbreaks around the world, including the severe acute respiratory syndrome (SARS) pandemic of 2002-2003 and the Middle East respiratory syndrome (MERS) outbreak in South Korea in 2015. Most recently, a novel coronavirus (SARS-CoV-2, also known as COVID-19) sparked an outbreak in China in December 2019, causing international epidemics. While some coronaviruses have caused devastating epidemics, others cause mild to moderate respiratory infections, like the common cold (ShrikrushnaS *et al,* 2020).

COVID-19: A REVIEW OF ITS GENECTIC STRUCTURE AND PATHOGENESIS.

GENETICAL STRUCTURE OF SARS-COV 2 (COVID-19).

SARS-CoV-2 (Covid-19) is a novel group 2b beta-coronavirus of the subgenus sarbecovirus, Orthocoronaviridae subfamilies. It has at least 70% similarity in genetic sequence to SARS□CoV (Hui *et al,* 2020).

COVID-19 is a spherical or pleomorphic enveloped particles containing single-stranded (positive-sense) RNA associated with a nucleoprotein within a capsid comprised of matrix protein. The envelope bears club-shaped glycoprotein projections. Since it has been found out that SARS-CoV 2 has similar characteristics with other coronaviruses like MERS-CoV and SARS-CoV, then its genetic structure is similar too.

Coronaviruses possess the largest genomes (26.4-31.7 kb) among all known RNA viruses, with G þ C contents varying from 32% to 43%. Variable numbers of small Overlapping Reading Frame (ORFs) are present between the various conserved genes (ORF1ab, spike, envelope, membrane and nucleo□capsid) and downstream to the nucleocapsid gene in different coronavirus lineages. The viral genome contains distinctive features, including a unique N-terminal fragment within the spike protein. Genes for the major structural proteins in all coronaviruses occur in the 5'-3' order as S, E, M, and N (Woo *et al*, 2010). A typical Coronavirus contains at least six ORFs in its genome.

Except for Gamma coronavirus that lacks nsp1, the first ORFs (ORF1a/b), about two-thirds of the whole genome length, encode 16 nsps (nsp1-16). ORF1a and ORF1b contain a frameshift in between which produces two polypeptides:

- pp1a
- pp1ab.

These polypeptides are processed by virally encoded chymotrypsin-like protease (3CLpro) or main protease (Mpro) and one or two papain-like protease into 16nsps. All the structural and accessory proteins are translated from the segmented RNAs of Coronavirus. Four main structural proteins contain spike (S), membrane (M), envelope (E), and nucleocapsid (N) proteins are encoded by Overlapping Reading Frames (ORFs) 10, 11 on the one-third of the genome near the 30-terminus (van Boheemen *et al*, 2012) (Czub M *et al*, 2005). Besides these four main structural proteins, different coronavirus encode special structural and accessory proteins, such as Hemagglutininin Esterase protein, 3a/b protein, and 4a/b protein. These mature proteins are responsible for several important functions in genome maintenance and virus replication (van Boheemen *et al*, 2012).

There are three or four viral proteins in the coronavirus membrane. The most abundant structural protein is the membrane (M) glycoprotein; it spans the membrane bilayer three times, leaving a short NH2-terminal domain outside the virus and a long COOH terminus (cytoplasmic domain) inside the virion (de Haan CAM *et al*, 1998). The spike protein (S) as a type I membrane glycoprotein constitutes the peplomers. In fact, the main inducer of neutralizing antibodies is Spike protein. Between the envelope proteins with exist a molecular interaction that probably determines the formation and composition of the coronaviral membrane. Membrane plays a predominant role in the intracellular formation of virus particles without requiring Spike protein. In the presence of tunica-mycin, coronavirus grows and produces spikeless, non-infectious virions that contain Membrane but devoid of Spike protein (Woo *et al,* 2010).

Basically, there are 2 main distinct differences that has been identified between SARS-COV 2 and other coronaviruses after several studies and analysis. They are...

- High affinity of SARS-COV 2 to Angiotensin converting enzyme 2 (ACE 2) in its pathogenicity.
- The furin-like cleavage site of Spike (S) glycoprotein of SARS-COV 2

HIGH AFFINITY TO ACE 2 IN THE PATHOGENICITY OF SARS-COV 2 TO OTHER CORONAVIRUSES.

The pathogenicity of SARS-COV 2 (COVID-19) is one of the major difference between it and other coronaviruses. Interestingly, several studies and analysis from samples collected from infected SARS-COV 2 patients have shown that SARS-CoV-2 uses angiotension converting enzyme 2 (ACE2) as its receptor, in common with SARS CoV (Hoffmann M *et al*, 2020). Coronaviruses mainly recognize their corresponding receptors on target cells through Spike proteins on their surface entry to the cells results in infection. A structure model analysis shows that SARS-CoV-2 binds to ACE2 with more than 10-fold higher affinity than SARS-CoV, at a level above the threshold required for virus infection (Wrapp D *et al,* 2020).

SARS-CoV-2 (COVID-19) binds to ACE2 (the angiotensin converting enzyme 2) by its Spike protein and allows COVID-19 to enter and infect cells. In order for the virus to complete entry into the cell following this initial process, the spike protein has to be primed by an enzyme called a protease. Similar to SARS-CoV, SARS-CoV-2 (COVID-19) uses a protease called TMPRSS2 to complete this process (Hoffmann M *et al,* 2020: Guo *et al,* 2020). In order toattach virus receptor (spike protein) to its cellular ligand (ACE2), activation by TMPRSS2 as a protease is needed (Hoffmann M *et al*, 2020). After the virus enters the host cell and uncoats itself, the genome of the virus is transcribed and then translated in the host. Coronavirus genome replication and transcription takes place at cytoplasmic membranes of the host and they involve coordinated processes of both continuous and discontinuous RNA synthesis that are mediated by the viral replicate, a huge protein complex encoded by the 20-kb replicase gene (Sola *et al,* 2015). The replicase complex is believed to be comprised of up to 16 viral sub units and a number of cellular proteins. Besides the RNA dependent RNA polymerase, RNA helicase, and protease activities, which are common to RNA viruses, the corona virus replicase was recently discovered to employ a variety of RNA processing enzymes that are not found in other RNA viruses and include putative sequence-specific endoribonuclease, 30-to-50 exoribonuclease, 20-O-ribose methyltransferase, ADP ribose 10-phosphatase and, in a subset of group 2 coronaviruses, cyclicphosphodiesterase activities (Ziebuhr j, 2005: Almaza'n *et al*, 2006). The proteins are assembled at the cell membrane and genomic RNA is incorporated as the mature particle forms by budding from the internal cell membranes (McIntosh and Peiris, 2009).

These studies explain the faster transmission capability of SARS-CoV-2 in humans compared with SARS-CoV, and the higher number of confirmed cases of COVID-19 compared with SARS-CoV infection. Considering the higher affinity of SARS-CoV-2 binding to ACE2, soluble ACE2 may be a potential candidate for the treatment of COVID-19.

THE FURIN-LIKE CLEAVAGE SITE OF SPIKE (S) GLYCOPROTEIN OF SARS-COV 2.

Coronavirus entry into host cells is facilitated by the trans-membrane spike (S) glycoprotein that forms homotrimers that protrudes from the viral surface (Tortorici and Veesler, 2019). S glycoprotein consist of two functional subunits which are:

- S1 subunit: Responsible for binding to the host cell receptor.
- S2 subunit: Responsible for the fusion of the viral and cellular membranes.

For many Coronaviruses, S is cleaved at the boundary between the S1 and S2 subunits, which remain non-covalently bound in the prefusion conformation (Burkard *et al.*, 2014; Kirchdoerfer *et al,* 2016; Millet and Whittaker, 2014).

The distal S1 subunit consist of the receptor-binding domain(s) and contributes to stabilization of the prefusion state of the membrane-anchored S2 subunit that contains the fusion machinery (Gui *et al.,* 2017; Pallesen *et al.,* 2017; Song *et al.,* 2018).

For all coronaviruses, S is further cleaved by host proteases at the so-called S2 subunit site located immediately upstream of the fusion peptide (Madu *et al.*, 2009; Millet and Whittaker, 2015). This cleavage has been proposed to activate the protein for membrane fusion through extensively irreversible conformational changes (Belouzard *et al*., 2009; Heald-Sargent and Gallagher, 2014; Park *et al.*, 2016; Walls *et al.*, 2017).

Different coronaviruses use distinct domains within the S1 subunit to recognize different types of attachment and entry receptors, depending on the viral species, for example, SARS-CoV and several SARS-related coronaviruses (SARSr-CoV) interact directly with angiotensin-converting enzyme 2 (ACE2) through S1 subunit boundary to enter target cells (Ge *et al.*, 2013; Kirchdoerfer *et al.*, 2018; Song *et al.,* 2018; Yang *et al.,* 2015).

The SARS-CoV-2 S1 subunit boundary engages human Angiotensin Converting Enzyme 2 (hACE2) with comparably higher affinity to SARS-CoV S1 subunit boundary from viral isolates associated with the 2002–2003 epidemic. Tight binding of SARS-COV 2 S1 subunit boundary to hACE2 could partially explain the efficient transmission of SARS-CoV-2 in humans. During the study process, the presence of an unexpected furin cleavage site at the S1-S2 boundary of SARS-CoV-2 Subunit which is cleaved during biosynthesis was identified. This furin-like cleavage site is a novel feature that distinguish SARS-CoV 2 from SARS-CoV and SARS-CoVs. Termination of this

cleavage motif moderately affected SARS-CoV-2 S-mediated entry into VeroE6 or BHK cells and may probably contribute to expand the tropism of this virus, as reported for several highly pathogenic avian influenza viruses and pathogenic Newcastle disease virus (Klenk and Garten, 1994; Steinhauer, 1999).

CONCLUSION.

Analytical studies and report have shown that the reason why SARS-COV 2 (COVID-19) is different from other coronaviruses is due to the accelerated level of its pathogenicity between humans which is due to it high affinity for Angiotensin Converting Enzyme 2 (ACE 2) and the fusin-like cleavage on the Spike glycoprotein. Though many research are still underway to detect more reason why COVID-19 is different, this two distinct features are enough to operate with for now until further studies are done and new discoveries are made.

REFERENCE.

Almaza´n F, DeDiego ML, Gala´n C, Escors D, A´lvarez E, Ortego J et al. (2006). Construction of a severe acute respiratory syndrome coronavirus infectious cDNA clone and a replicon to study coronavirus RNA synthesis. J Virol; 80(21): 10900-6

Belouzard, S., Chu, V.C., and Whittaker, G.R. (2009). Activation of the SARS coronavirus spike protein via sequential proteolytic cleavage at two distinct sites. Proc. Natl. Acad. Sci. USA; 106: 5871–5876.

Burkard, C., Verheije, M.H., Wicht, O., van Kasteren, S.I., van Kuppeveld, F.J.,Haagmans, B.L., Pelkmans, L., Rottier, P.J., Bosch, B.J., and de Haan, C.A. (2014). Coronavirus cell entry occurs through the endo-lysosomal pathway in a proteolysis-dependent manner. PLoS Pathog: 10; 1004502.

Czub M, Weingartl H, Czub S, He R, Cao J. (2005). Evaluation of modified vaccinia virus Ankara based recombinant SARS vaccine in ferrets. Vaccine; 23(17-18):2273-9.

de Haan CAM, Kuo L, Masters PS, Vennema H, Rottier PJM. (1998). Coronavirus particle assembly: primary structure requirements of the membrane protein. J Virol; 72(8):6838-50

Drosten C, Günther S, Preiser W.(2020). Identification of a novel coronavirus in patients with severe acute respiratory syndrome. Engl J Med; 348: 1967–76.

Ge, X.Y., Li, J.L., Yang, X.L., Chmura, A.A., Zhu, G., Epstein, J.H., Mazet, J.K., Hu, B., Zhang, W., Peng, C., et al. (2013). Isolation and characterization of a bat SARS-like coronavirus that uses the ACE2 receptor. Nature; 503: 535–538.

Gui, M., Song, W., Zhou, H., Xu, J., Chen, S., Xiang, Y., and Wang, X. (2017). Cryo-electron microscopy structures of the SARS-CoV spike glycoprotein reveal a prerequisite conformational state for receptor binding. Cell Res; 27:119–129.

Guo Y-R, Cao Q-D, Hong Z-S, Tan Y-Y, Chen S-D, Jin H-J, et al. (2020). The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreake: an update on the status. Mil Med Res; 7(1):1-10

Heald-Sargent, T., and Gallagher, T. (2014). Ready, set, fuse! The corona virus spike protein and acquisition of fusion competence. Viruses; 4: 557–580.

Hoffmann M, Kleine-Weber H, Krüger N, Müller M, Drosten C, Pöhlmann S. (2020). The novel coronavirus 2019 (2019-nCoV) uses the SARS-coronavirus receptor ACE2 and the cellular protease TMPRSS2 for entry into target cells. bioR xiv 2020.01.31.929042.

Hui DS, I. Azhar E, Madani TA, Ntoumi F, Kock R, Dar O, et al. (2020). The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health - The latest 2019 novel coronavirus outbreak in Wuhan, China. PubMed Int J Infect Dis; 91: 264–6.

Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, *et al.* (2020). Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet; 395: 497–506.

Kirchdoerfer, R.N., Cottrell, C.A., Wang, N., Pallesen, J., Yassine, H.M.,Turner, H.L., Corbett, K.S., Graham, B.S., McLellan, J.S., and Ward, A.B. (2016). Pre-fusion structure of a human coronavirus spike protein. Nature; 531: 118–121.

Kirchdoerfer, R.N., Wang, N., Pallesen, J., Wrapp, D., Turner, H.L., Cottrell, C.A., Corbett, K.S., Graham, B.S., McLellan, J.S., and Ward, A.B. (2018). Stabilized coronavirus spikes are resistant to conformational changes induced by receptor recognition or proteolysis. Sci. Rep; 8: 15701.

Klenk H.D., and Garten W. (1994). Host cell proteases controlling virus pathogenicity. Trends Microbiol; 2: 39–43

Madu, I.G., Roth, S.L., Belouzard, S., and Whittaker, G.R. (2009). Characterization of a highly conserved domain within the severe acute respiratory syndrome coronavirus spike protein S2 domain with characteristics of a viral fusion peptide. J. Virol; 83: 7411–7421.

McIntosh K, Peiris JSM. (2009). Coronaviruses. Clinical virology. 3rd ed. American Society of Microbiology; pg. 1155-71.

Millet, J.K., and Whittaker, G.R. (2014). Host cell entry of Middle East respiratory syndrome coronavirus after two-step, furin-mediated activation of the spike protein. Proc. Natl. Acad. Sci. USA 111, 15214–15219.

Pallesen, J., Wang, N., Corbett, K.S., Wrapp, D., Kirchdoerfer, R.N., Turner,H.L., Cottrell, C.A., Becker, M.M., Wang, L., Shi, W., et al. (2017). Immunogenicity and structures of a rationally designed prefusion MERS-CoV spike antigen. Proc. Natl. Acad. Sci. USA 114, E7348–E7357.

Park, Y.J., Walls, A.C., Wang, Z., Sauer, M.M., Li, W., Tortorici, M.A., Bosch,B.J., DiMaio, F., and Veesler, D. (2019). Structures of MERS-CoV spike glycoprotein in complex with sialoside attachment receptors. Nat. Struct. Mol. Biol; 26: 1151–1157.

Shrikrushna Subhash Unhale, Quazi Bilal Ansar, Shubham Sanap , Suraj Thakhre, Shreya Wadatkar, Rohit Bairagi, Prof. Suraj Sagrule and Prof. Dr. K. R. Biyani. (2020).A review on corona virus (covid-19). Wjpls; vol 6: 109-115.

Sola I, Almazan F, Zuniga S, Enjuanes L. (2015). Continuous and discontinuous RNA synthesis in coronaviruses. Ann Rev Virol; 2: 265-88.

Song, W., Gui, M., Wang, X., and Xiang, Y. (2018). Cryo-EM structure of the SARS coronavirus spike glycoprotein in complex with its host cell receptor ACE2. PLoS Pathog: 14: 1007236.

Steinhauer D.A. (1999). Role of hemagglutinin cleavage for the pathogenicity of influenza virus. Virology; 258: 1–20.

Tortorici, M.A., and Veesler, D. (2019). Structural insights into coronavirus entry. Adv. Virus Res; 105: 93–116

Van Boheemen S, de Graaf M, Lauber C, Bestebroer TM, Raj VS, Zaki AM, et al. (2012). Genomic characterization of a newly discovered coronavirus associated with acute respiratory distress syndrome in humans. mBio; 3(6): 00473-12

Walls, A.C., Tortorici, M.A., Snijder, J., Xiong, X., Bosch, B.-J., Rey, F.A., and Veesler, D. (2017). Tectonic conformational changes of a coronavirus spike glycoprotein promote membrane fusion. Proc. Natl. Acad. Sci. USA; 114: 11157–11162

Weiss SR, Leibowitz JL. (2011). Coronavirus pathogenesis. Adv Virus Res; 81: 85–164.

Woo PCY, Huang Y, Lau SKP, Yuen K-Y. (2010). Coronavirus genomics and bioinformatics analysis. Viruses; 2(8): 1804-20.

Wrapp D, Wang N, Corbett KS, Goldsmith JA, Hsieh CL, Abiona O, et al. Cry□o-EM structure of the 2019-nCoV spike in the prefusion conformation. Science (New York, NY); 367(6483):1260–3

Yang D, Leibowitz JL. (2015). The structure and functions of coronavirus genomic 3’ and 5’ ends. Virus Res; 206:120–33.

Yang X.L., Hu B., Wang, B., Wang, M.N., Zhang, Q., Zhang, W., Wu, L.J., Ge X.Y., Zhang Y.Z., Daszak, P., et al. (2015). Isolation and Characterization of a Novel Bat Coronavirus Closely Related to the Direct Progenitor of Severe Acute Respiratory Syndrome Coronavirus. J. Virol; 90: 3253–3256.

Ziebuhr J. (2015). The coronavirus replicase. Coronavirus replication and reverse genetics. Springer; pg 57-94.