Popular Article

THE SCIENCE WORLD
A Monthly e Magazine

ISSN:2583-2212
November, 2022; 2(11), 1979-1983

Covid-19: Novel Coronavirus Structure and Immune Response to Viral Infection

Dhaval J Kamothi[1]*, Manju Gari[2], K. Lalawmpuii[3], Shubham Kumar[4] and Dinesh Kumar[5]

[1]Ph.D. Scholar, Division of Pharmacology and Toxicology, ICAR-Indian Veterinary Research Institute, Izatnagar, Bareilly, U.P., 243122

[2]Ph.D. Scholar, Division of Pharmacology and Toxicology, ICAR-Indian Veterinary Research Institute, Izatnagar, Bareilly, U.P., 243122

[3]Ph.D. Scholar, Department of Veterinary Parasitology, College of Veterinary Science, Guru Angad Dev Veterinary and Animal Sciences University, Ludhiana

[4]Ph.D. Scholar, Division of Pharmacology and Toxicology, ICAR-Indian Veterinary Research Institute, Izatnagar, Bareilly, U.P., 243122

[5]Principal Scientist & Head, Division of Pharmacology & Toxicology, ICAR-Indian Veterinary Research Institute, Izatnagar, 243122, U.P, India

https://doi.org/10.5281/zenodo.7404696

Introduction

The world has confronted a number of pandemics in the past, and after the 1918 flu pandemic, the world is again facing a similar situation. In nature, numerous mysteries regarding viruses remain unresolved and Novel Coronavirus is one of them. Coronaviruses are RNA viruses that are known to cause diseases in animals and humans. They are mainly responsible for respiratory and intestinal infections. In 2002-2003, outbreaks of severe acute respiratory syndrome (SARS) caused the mortality of more than 770 people worldwide (Drosten *et al*., 2003), followed by the outbreak of the Middle East respiratory syndrome (MERS), both the diseases caused by the coronavirus belonging to the genus beta coronavirus (Singh *et al*., 2020). On December 31, 2019, local hospitals in china and the Centers for Disease Control and Prevention reported many instances of pneumonia of unclear origin, and the illness was ultimately traced to a seafood market in Wuhan, Hubei Province, China (Zhu *et al*., 2020). World Health Organization (WHO) on January 12th, 2020 named the virus SARS-CoV-2 and the disease COVID-19 on 11th February 2020. On March 11, 2020, the novel coronavirus (COVID-19) outbreak was declared a global pandemic by WHO. The virus primarily affects the respiratory system, causing flu-like symptoms such as fever, coughing, and, in more severe cases, difficulty breathing (Zou *et al*., 2020). The majority of patients recover in 1–3 weeks, but about 5% develop severe symptoms that can lead to acute respiratory distress syndrome (ARDS) and respiratory failure, which can lead to death.

Furthermore, COVID-19 may cause systemic inflammation in high-risk patients, placing them at risk of sepsis, cardiovascular problems, and organ failure (Wang *et al*., 2020). People over the age of 60 and those with other morbidities are at a higher risk of mortality (Wang *et al*., 2020).

Novel Coronavirus Structure

SARS-CoV-2 is an enveloped, positive-sense RNA virus (Zhu *et al*., 2020) and has a diameter of around 50-200nm. The viral structure consists of four structural proteins, which are known as S (spike), E (envelope), M (membrane), and N (nucleocapsid) proteins (Fig. 1). The viral genome (RNA) is held by the N protein, while the viral envelope is formed together by S, E, and M proteins. The viral M protein provides the virus its shape while the E protein aids in the viral release from the infected cells (Ashour *et al*., 2020). The genome of the SARS-CoV-2 is approximately 25–31 kb in size and virus has a spherical morphology containing 9,860 amino acids. The SARS-CoV-2 exhibits high similarity in sequence with the bat-SL-CoVZC45 (88%) and bat-SL-CoVZXC2 (87%), while it presents less similarity with the SARS-CoV-1 (79%) and MERS-CoV (50%) (Lu *et al*., 2020). Having an advantage of such large genome, novel coronavirus can produce more proteins one of which is an enzyme called exonuclease (ExoN) allowing virus to proofread and correct copies as they are made.

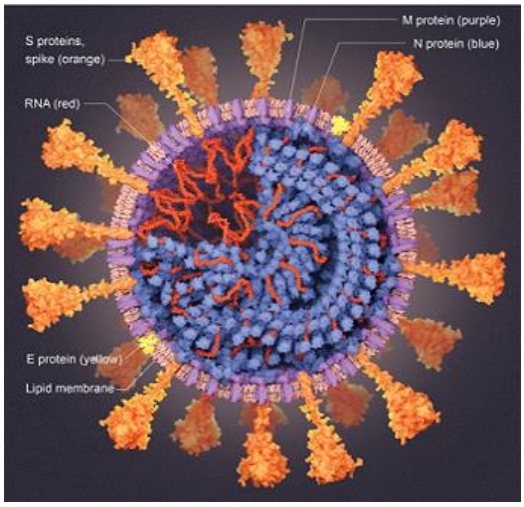

Fig. 1. SARS-CoV-2 viral structure [Image Source: Lorenzo Casalino, Zied Gaieb and Rommie Amaro, U.C. San Diego (*spike model with glycosylations*)]

Immune response to SARS-CoV-2

The transmission of the virus occurs from human to human mainly through inhalation route and the virus passes through the respiratory tract and floats until it brushes against a lung cell consisting of angiotensin Angiotensin-converting enzyme receptor 2 (ACE2) on the cellular surface and S2' site. Upon interaction with the ACE2 receptor, the spike protein of the virus binds with the receptor resulting into the transmembrane serine protease 2 (TMPRSS2) mediated cleavage of spike protein subunit at

S1/S2 site.

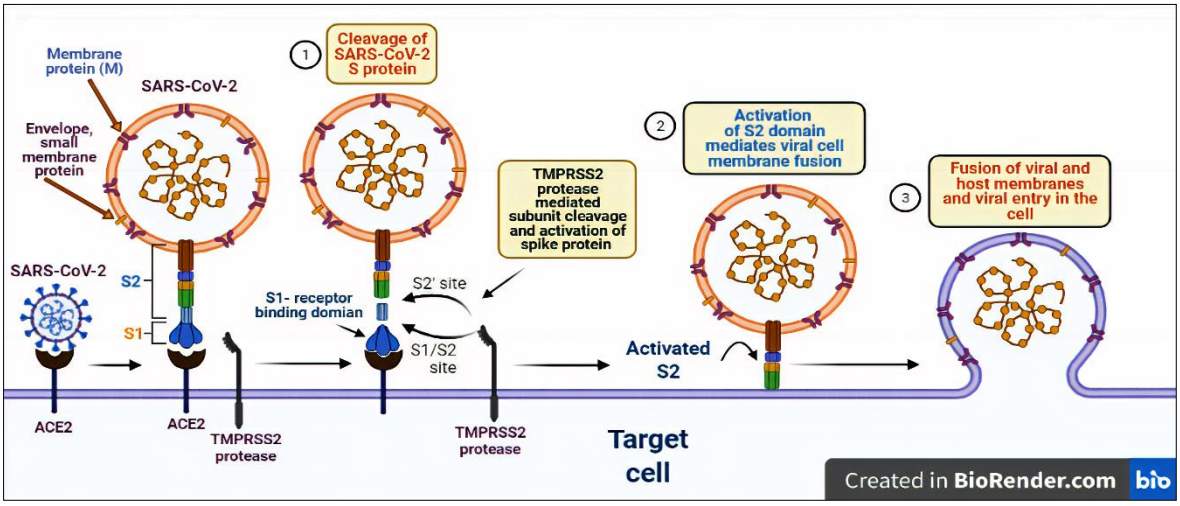

Fig. 2. Interaction of SARS-CoV-2 with ACE2 receptor [Pictorial representation is designed manually by using an online tool (Biorender)]

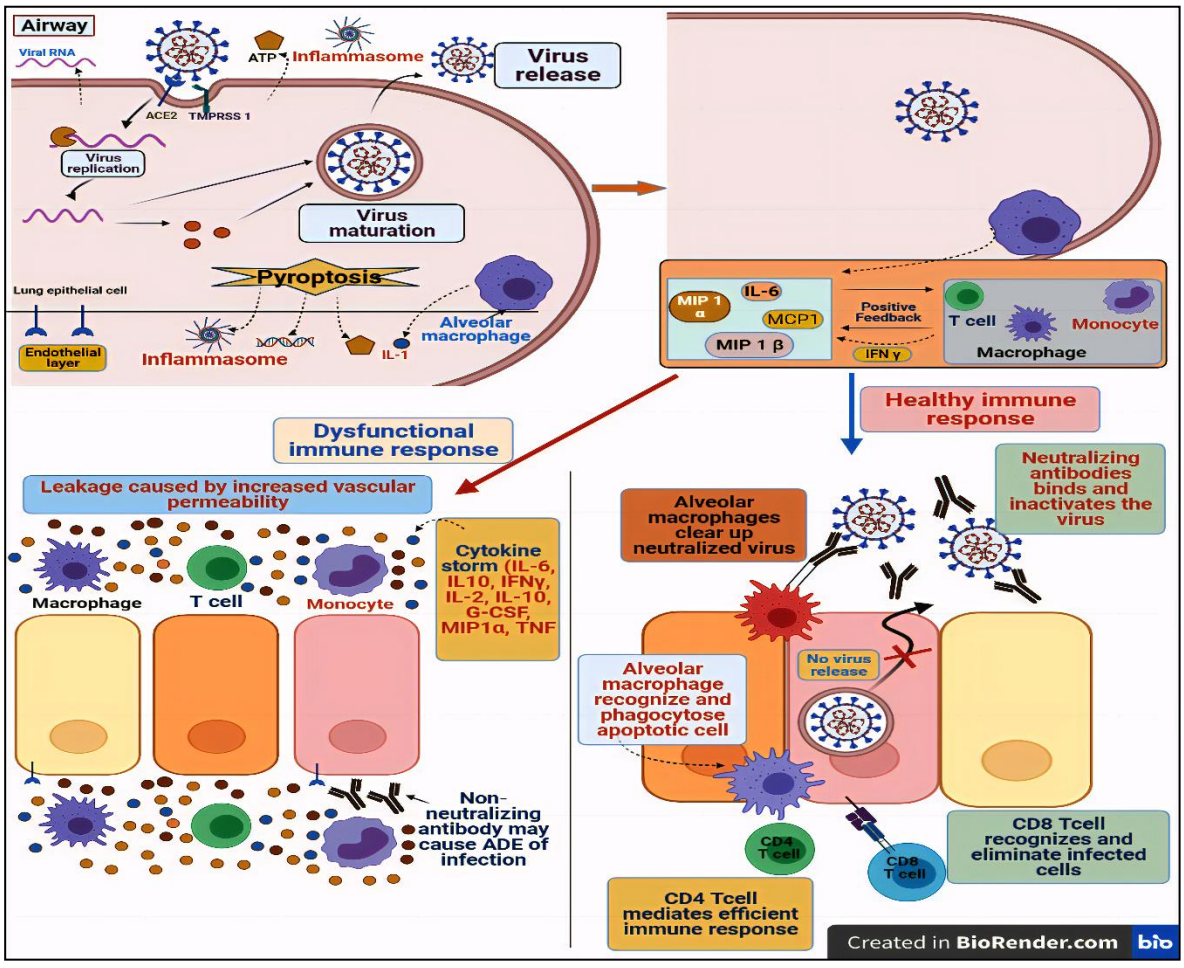

Fig. 3. Immune response to SARS-CoV-2 infection [Pictorial representation is designed manually by using an online tool (Biorender)]

The viral S1 subunit has two domains: one is amino-terminal domain and another is receptor binding domain (RBD). The binding to the ACE2 receptor occurs through RBD, thereby triggering the process of endocytosis of the SARS-CoV-2 virion (Fig. 2). This leads to activation of the S2 subunit which consist of fusion peptide (FP) region and two heptad repeat regions: HR1 and HR2. Now the S1 subunit is cleaved away exposing the FP region of the, upon which the S2 region folds in on itself to bring the HR1 and HR2 regions together, resulting in membrane fusion and releases the virus into the host cytoplasm (Fig. 2).

Following the viral entry and replication inside the host cell, viral recognition occurs by pattern recognition receptors (PRR) such as Toll-like receptors and viral-infection sensors Retinoic acid-Inducible Gene I protein (RIG-I) and Melanoma Differentiation-Associated protein 5 (MDA5) (Prompetchara *et al*., 2020). TLR3 activation causes transcription of the NLP3 gene, which causes the NLRP3 inflammasome to activate (Nieto-Torres *et al*., 2015). The activated NLRP3 inflammasome is responsible for the cleavage through caspase-1, which results in activation and release of pro-inflammatory cytokines such as IL-1β and IL-18, and further leads to activation of gasdermin D-mediated pyroptotic cell death and release damage-associated molecular patterns (DAMPs), including ATP, nucleic acids and ASC oligomers. Neighbouring epithelial cells, endothelial cells, and alveolar macrophages identify this, triggering the production of IL-6, IP-10, macrophage inflammatory protein 1α (MIP1α), MIP1β and MCP1 **(**Tay *et al*., 2020). The release of these proteins attracts monocytes, macrophages, and T cells to the infection site, causing further inflammation and IFN production by T cells, resulting in a pro-inflammatory feedback loop. A faulty immune response leads to an accumulation of immune cells in the lungs, which causes an overproduction of pro-inflammatory cytokines, causing lung infrastructure damage (Fig. 3). Inflammatory responses may be exacerbated when Th1/Th17 cells are stimulated with viral epitopes. "Cytokine storms" are the outcome of this inflammatory response. The cytokine storm that results produces pulmonary edema and pneumonia, and it spreads to other organs, causing multi-organ damage. Furthermore, non-neutralizing antibodies produced by B cells may promote SARS-CoV-2 infection via antibody-dependent enhancement (ADE), aggravating even more organ damage.

Conclusion

The Covid 19 declared as the global pandemic by WHO caused by SARS-CoV-2 virus affects mainly the respiratory system leading to anoxia and pulmonary fibrosis as a result of aggravated immune response forming a ‘cytokine storm’, which involves presence number of cytokines, inflammatory cells and growth factors, leading to development of acute respiratory distress syndrome

(ARDS) and respiratory failure, which can lead to fatal consequences.

References

Ashour, H. M., Elkhatib, W. F., Rahman, M. M., & Elshabrawy, H. A. (2020). Insights into the recent 2019 novel coronavirus (SARS-CoV-2) in light of past human coronavirus outbreaks. *Pathogens*, *9*(3), 186.

Drosten, C., Günther, S., Preiser, W., Van Der Werf, S., Brodt, H. R., Becker, S., ... & Doerr, H. W. (2003). Identification of a novel coronavirus in patients with severe acute respiratory syndrome. *New England journal of medicine*, *348*(20), 1967-1976.

Lu, R., Zhao, X., Li, J., Niu, P., Yang, B., Wu, H., ... & Tan, W. (2020). Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *The lancet*, *395*(10224), 565-574.

Nieto-Torres, J. L., Verdiá-Báguena, C., Jimenez-Guardeño, J. M., Regla-Nava, J. A., Castaño-Rodriguez, C., Fernandez-Delgado, R., ... & Enjuanes, L. (2015). Severe acute respiratory syndrome coronavirus E protein transports calcium ions and activates the NLRP3 inflammasome. *Virology*, *485*, 330-339.

Prompetchara, E., Ketloy, C., & Palaga, T. (2020). Immune responses in COVID-19 and potential vaccines: Lessons learned from SARS and MERS epidemic. *Asian Pacific journal of allergy and immunology*, *38*(1), 1-9.

Singh, A., Shaikh, A., Singh, R., & Singh, A. K. (2020). COVID-19: From bench to bed side. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*, *14*(4), 277-281.

Tay, M. Z., Poh, C. M., Rénia, L., MacAry, P. A., & Ng, L. F. (2020). The trinity of COVID-19: immunity, inflammation and intervention. *Nature Reviews Immunology*, *20*(6), 363-374.

Wang, D., Hu, B., Hu, C., Zhu, F., Liu, X., Zhang, J., ... & Peng, Z. (2020). Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. *Jama*, *323*(11), 1061-1069.

Zhu, N., Zhang, D., Wang, W., Li, X., Yang, B., Song, J., ... & Tan, W. (2020). A novel coronavirus from patients with pneumonia in China, 2019. *New England journal of medicine*.

Zou, L., Ruan, F., Huang, M., Liang, L., Huang, H., Hong, Z., ... & Wu, J. (2020). SARS-CoV-2 viral load in upper respiratory specimens of infected patients. *New England journal of medicine*, *382*(12), 1177-1179.