International Journal of Biology Research
ISSN: 2455-6548; Impact Factor: RJIF 5.22
Received: 28-04-2020; Accepted: 08-05-2020; Published; 29-05-2020
www.biologyjournal.in
Volume 5; Issue 2; 2020; Page No. 09-11

Novel Corona Virus Outbreak (Covid-19): Its Genomic Structure And Treatments

Swapnil Mawal
Research Scholar, Department of Environmental Sciences, Savitribai Phule Pune University, Pune, Maharashtra, India

Abstract
Novel Coronavirus Disease (COVID-19) is a highly infectious disease. The outbreak was first detected in Wuhan City, Hubei Province of China and become a pandemic due to its very high transmission rate. The current paper highlights the scenario of coronavirus outbreak and its genomic structure and treatments. The objective of the study is to explore and extract the information originated from various studies on the infection outbreak, criteria of diagnosis, and antiviral treatments from 2019-nCov infection.

Keywords: Coronavirus (Covid-19), genomic structure, pandemic, treatments.

1. Introduction

Coronaviruses (CoVs) are the largest group of viruses belonging to the Nidovirales order, which includes Coronaviridae, Arteriviridae, and Roniviridae families. The Coronavirinae comprise one of two subfamilies in the Coronaviridae family, with the other being the Torovirinae. The Coronavirinae are further subdivided into four groups, the alpha, beta, and gamma and delta coronaviruses. The viruses were initially sorted into these groups based on serology but are now divided by phylogenetic clustering. Coronaviruses are enveloped non-segmented positive-sense RNA viruses belonging to the family Coronaviridae and the order Nidovirales and broadly distributed in humans and other mammals. Although most human coronavirus infections are mild, the epidemics of the two beta coronaviruses, severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) have caused more than 10 000 cumulative cases in the past two decades, with mortality rates of 10% for SARS-CoV and 37% for MERS-CoV.7, 8. The coronaviruses already identified might only be the tip of the iceberg, with potentially more novel and severe zoonotic events to be revealed. In December 2019, a series of pneumonia cases of unknown cause emerged in Wuhan, Hubei, China, with clinical presentations greatly resembling viral pneumonia. Deep sequencing analysis from lower respiratory tract samples indicated a novel coronavirus, which was named 2019 novel coronavirus (2019-nCoV). Thus far, more than 800 confirmed cases, including in health-care workers, have been identified in Wuhan, and several exported cases have been confirmed in other provinces in China, and Thailand, Japan, South Korea, and the USA.10–13. (Huang *et al*, 2020, Wrapp *et al*, 2020, Upreti *et al*, 2020) [3, 5, 4].

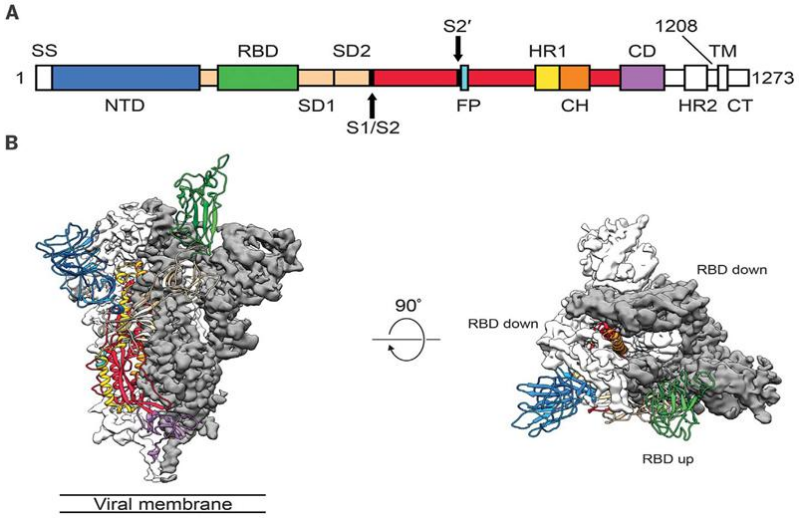

Fig 1: Structure of 2019-nCoV S in the prefusion conformation. (A) Schematic of 2019-nCoV S primary structure coloured by domain. Domains that were excluded from the ectodomain expression constructor could not be visualized in the final map are coloured white. SS, signal sequence; S2′, S2′ protease cleavage site; FP, fusion peptide; HR1, heptad repeat 1; CH, central helix; CD, connector domain; HR2, heptad repeat 2; TM, transmembrane domain; CT, cytoplasmic tail. Arrows denote protease cleavage sites. (B) Side and top views of the prefusion structure of the 2019-nCoV S protein with a single RBD in the up conformation. The two RBD down protomers are shown as cryo-EM density in either white or grey and the RBD up protomer is shown in ribbons coloured corresponding to the schematic in (A) (Adopted from Wrapp *et al*, 2020) [5].

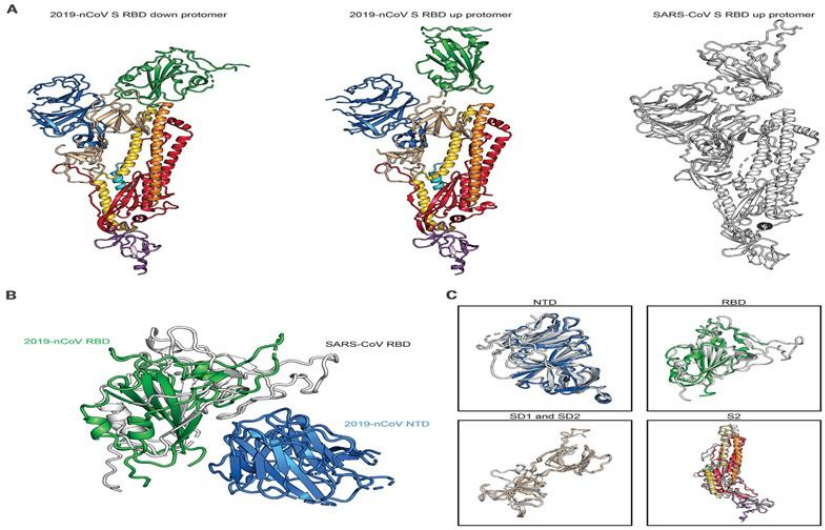

Fig 2: Structural comparison between 2019-nCoV S and SARS-CoV S. (A) Single protomer of 2019-nCoV S with the RBD in the down conformation (left) is shown in ribbons coloured according to Fig. 1. A protomer of 2019-nCoV S in the RBD up conformation is shown (centre) next to a protomer of SARS-CoV S in the RBD up conformation (right), displayed as ribbons and coloured white (PDB ID: 6CRZ). (B) RBDs of 2019-nCoV and SARS-CoV aligned based on the position of the adjacent NTD from the neighbouring protomer. The 2019-nCoV RBD is coloured green and the SARS-CoV RBD is coloured white. The 2019-nCoV NTD is coloured blue. (C) Structural domains from 2019-nCoV S have been aligned to their counterparts from SARS-CoV S as follows: NTD (top left), RBD (top right), SD1 and SD2 (bottom left), and S2 (bottom right). (Adopted From Wrapp *et al*, 2020) [5].

1.2 Genomic Organization

Coronaviruses contain a non-segmented, positive-sense RNA genome of ~30 kb. The genome contains a 5′ cap structure along with a 3′ poly (A) tail, allowing it to act as a mRNA for translation of the replicase polyproteins. The replicase gene encoding the non-structural proteins (Nsps) occupies two-thirds of the genome, about 20 kb, as opposed to the structural and accessory proteins, which make up only about 10 kb of the viral genome. The 5′ end of the genome contains a leader sequence and untranslated region (UTR) that contains multiple stem-loop structures required for RNA replication and transcription. Additionally, at the beginning of each structural or accessory gene are transcriptional regulatory sequences (TRSs) that are required for expression of each of these genes (see the section on RNA replication). The 3′UTR also contains RNA structures required for replication and synthesis of viral RNA. The organization of the coronavirus genome is 5′-leader-UTR-replicase-S (Spike)–E (Envelope)-M (Membrane)-N (Nucleocapsid)-3′UTR-poly (A) tail with accessory genes interspersed within the structural genes at the 3′ end of the genome. The accessory proteins are almost exclusively non-essential for replication in tissue culture; however, some have been shown to have important roles in viral pathogenesis. (Upreti et al, 2020, Wrapp et al, 2020) [5, 4].

1.3 Treatment of COVID-19

1.3.a. Current therapies

Given the lack of effective antiviral therapy against COVID-19, current treatments mainly focused on symptomatic and respiratory support according to the Diagnosis and Treatment of Pneumonia Caused by COVID-19 issued by National Health Commission of the People's Republic of China. Nearly all patients accepted oxygen therapy, and WHO recommended extracorporeal membrane oxygenation (ECMO) to patients with refractory hypoxemia. Rescue treatment with convalescent plasma and immunoglobulin G [73] are delivered to some critical cases according to their conditions.

1.3.b. Antiviral treatments

Based on the experience of fighting the epidemic SARS-CoV and MERS-CoV previously, we may learn some lessons for some treatment strategies against coronavirus. Antiviral drugs and systemic corticosteroid treatment commonly used in clinical practice previously, including neuraminidase inhibitors (oseltamivir, peramivir, zanamivir, etc), ganciclovir, acyclovir, and ribavirin, as well as methylprednisolone for influenza virus, are invalid for COVID-19 and not recommended. Remdesivir (GS-5734) is a 1′-cyano-substituted adenosine nucleotide analog prodrug and shows broadspectrum antiviral activity against several RNA viruses. Based on the data collected from in vitro cell line and mouse model, redeliver could interfere with the NSP12 polymerase even in the setting of intact ExoN proofreading activity. Remdesivir has been reported to treat the first US case of COVID-19 successfully. Chloroquine is a repurposed drug with great potential to treat COVID-19. Chloroquine has been used to treat malaria for many years with a mechanism that is not well understood against some viral infections. Several possible mechanisms are investigated: Chloroquine can inhibit pH-dependent steps of the replication of several viruses, with a potent effect on SARS-CoV infection and spread. Moreover, chloroquine has immunomodulatory effects, suppressing the production/release of TNF-α and IL-6. It also works as a novel class of autophagy inhibitor, which may interfere with viral infection and replication. Several studies have found that chloroquine interfered with the glycosylation of cellular receptors of SARS-CoV and functioned at both entries and post-entry stages of the COVID-19 infection in Vero E6 cells. A combination of remdesivir and chloroquine was proven to effectively inhibit the recently emerged SARS-CoV-2 in vitro. Scientists previously confirmed that the protease inhibitors lopinavir and ritonavir, used to treat the

infection with human immunodeficiency virus (HIV), could improve the outcome of MERS-CoV [84] and SARS-CoV patients. It has reported that β-coronavirus viral loads of a COVID-19 patient in Korea significantly decreased after lopinavir/ritonavir Additionally, clinicians combined Chinese and Western medicine treatment including lopinavir/ritonavir (Kaletra®), arbidol, and Shufeng Jiedu Capsule (SFJDC, a traditional Chinese medicine) and gained significant improvement in pneumonia associated symptoms in Shanghai Public Health Clinical Center, China. The other antiviral drugs include nitazoxanide. (Guo *et al*.2020).

References

1. Zhao L, Jha BK, Wu A, Elliott R, Ziebuhr J, Gorbalenya AE, Silverman RH, Weiss SR. Antagonism of the interferon-induced OAS-RNase L pathway by murine coronavirus ns2 protein is required for virus replication and liver pathology. Cell host & microbe. 2012; 11(6):607–616. [PubMed: 22704621].
2. Guo YR, Cao DN Sihong Z, Tan YY. The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak – an update on the Status. Military Medical Research, 2020. 7:11https://doi.org/10.1186/s40779-020-00240
3. Huang C, Wang Y. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet, 497–506.
4. Upreti BM, Bhatt S, BS Mengwal.. Worldwide Novel Corona Virus Outbreak (COVID-19). Journal of Science and Healthcare Exploration (JSHE). 2020; 2(2):14-17.
5. Wrapp D, Wang N, Corbett KS, A Goldsmith, Hsie CL, Abiona O, Graham BS, JS McLellan. CORONAVIRUS Cryo-EM structure of the 2019-nCoV spike in the prefusion conformation, Science. 2020; 367:1260–1263.
6. https://www.who.int/emergencies/diseases/novel-coronavirus.-2019/situation-reports