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Covid-19: A Paradigm from Origin to Treatment and Cure.

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Abstract

The corona virus disease-2019 (COVID-19) was caused by a newly emerged Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) in the last month of December, 2019 in Wuhan, China. The disease is responsible for the worldwide health emergency and economic crisis. The spike protein anchored on the virus membrane grants them crown-like appearance and facilitates their entry into target cell. In this commentary, we explore various aspects such as origin, morphology, inflammatory responses, treatment and cure of the disease in brief. According to the latest reports, Pfizer/BioNTech honoured the first in the world to discharge full late-stage trial data on November 18, 2020. Eight countries in the world have granted consent to vaccinate their people against the disease.

Keywords: COVID-19, SARS-CoV-2, Genome and Morphology, Inhibitors, Drug Repurposing, Treatment and Cure.

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Origin of the Disease

A virus is a small obligate intracellular parasite that comprise of nucleic acid (single or double stranded DNA or RNA) and a protein coat called capsid. The capsid safeguards the viral genome from nucleases and affixes the virion (a complete virus particle) to distinct receptors exposed on the host cell during infection. The main motif of the virion is to transmit its genome into the host cell so that the genome can be expressed by the host cell. A newly loomed pathogen, 2019 novel coronavirus (2019-nCoV), engendered an outbreak of communicable respiratory disease in December, 2019 in Wuhan, China [1]. The first complete sequence of the virus was released on January 10, 2020. The genome sequence assisted in the quick recognition of virus in patients by utilizing reverse transcription polymerase chain reaction (RTPCR) [1]. The World Health Organization (WHO) in perpetuity named the virus likely SARS-CoV-2 and the disease likely COVID-19 on February12, 2020. Originally, the disease cluster was associated to Huanan sea food market, apparently due to animal proximity. Afterwards, human-to-human transmission was reported and the disease swiftly spread globally. Because of global expansion, WHO declared the outbreak an epidemic on March 11, 2020. The disease has spread to 223 countries, territories or areas with 104,370,550 confirmed cases and 2,271,180 confirmed deaths worldwide as of February 5, 2021 [2]. The virus can infect both humans and other animals causing common cold, fatigue, fever, cough dyspnea and severe diseases including SARS and Middle East Respiratory Syndrome (MERS).

Although, bats that host a variety of CoVs were observed resistant to coronavirus-induced disease.

Genome and Morphology

CoVs have a positive-sense single-stranded RNA genome surrounded by a membrane envelope. The viral envelope is comprised of a lipid bilayer where the structural proteins including envelope (E), spike (S) and membrane (M) are fixed [3]. The spike protein implanted on the viral membrane grants them crown-like appearance (Figure 1). The size of genome ranging between 27 to 34 kb, the largest among RNA viruses. The genome of SARS-CoV-2 is comprised of ~ 30,000 nucleotides. Its replicase gene encodes pp1ab and pp1a, polyproteins which are crucial for viral replication and transcription [4]. The S protein of the CoVs make easy its entry into target cells. Numerous non-structural proteins including papain-like protease, main protease, and RNA-dependent RNA polymerase are also encoded by the viral genome. Cryo-EM results demonstrate 10–20 times greater binding affinity of SARS-CoV-2 S protein to angiotensin-converting enzyme 2 (ACE2) in contrast to SARS-CoV S protein [5]. In contrast to SARS-CoV and MERS-CoV, SARS-CoV-2 also effects gastrointestinal system, central nervous system, kidney, liver, and heart along with the lower respiratory system, leading to numerous organ failure [1]. SARS-CoV-2 is relatively large spherical or pleomorphic particle with bulbous surface extensions (Figure 1) [6]. The diameter of the viral particle was observed between 80 to 120 nm.

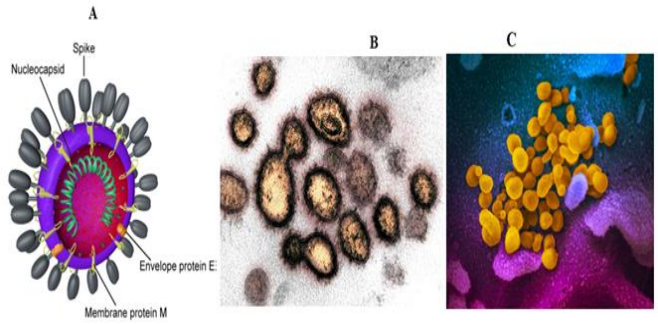

Figure 1. *A: Structure of SARS-CoV-2 displaying the presence of envelope (E), membrane (M), spike (S), and nucleocapsid (N) proteins. B: transmission electron microscopic depiction of SARS-CoV-2, manifesting spikes on the outer edge of the virus. C: scanning electron microscopic depiction of SARS-CoV-2 (Yellow), displaying pleomorphic or spherical shape of the virus. Reprinted with permission from Ref. [6]. Copyright 2021 Springer Science + Business Media.*

Inflammatory Responses

In agreement with the latest reports, both SARS-CoV and SARS-CoV-2 utilize ACE2 as entry receptor for infection which urges the possibility of the alike cells being targeted and infected by both the viruses. On the basis of recent investigations on SARS-CoV, the inflammatory responses in COVID-19 has been divided into primary and secondary responses. The primary inflammatory responses take place early after viral infection that is before the arrival of neutralizing antibodies (NAb) [7]. These responses are predominantly led by active viral replication, host antiviral responses and viral-induced ACE2 downregulation or shedding. The primary inflammatory responses include cytokine/chemokine release, expression of anti-viral factors, pulmonary cell infiltration, increased vascular permeability, lymphopenia, renin–angiotensin system dysfunction etc. The secondary inflammatory responses begin with the generation of adaptive immunity and NAb. The virus–NAb complex can also cause FcR-mediated inflammatory responses. The secondary inflammatory responses include skewing macrophage response, MCP-1 and IL-8 production, abrogating wound-healing responses, acute lung injury and cell damage.

Treatment of the Disease

The timely formation of functional antiviral drugs for clinical usage is highly challenging. The repurposing of officially valid pharmaceutical drugs and drug candidates propose an unorthodox method to quickly identify potential drug leads for handling of quickly emerging viral infections. The convergence of virtual screening, high-throughput screening and structure-based ab initio drug design methods proposes a new way to locate new drugs for treating COVID-19. l drugs. Moreover, repurposing of already available drugs to treat COVID-19 provides as one of the economical and efficient therapeutic strategies. Owing to anti-inflammatory sequel and high capability to hinder viral entry, baricitinab was considered as the potential drug for the treatment COVID-19 [9]. Remdesivir (RDV) has been lately recognized as a promising antiviral drug against a wide range of RNA viruses including SARS and MERS-CoV. It is presently under clinical testing for treating Ebola virus disease [9]. An authorized dose of anti-HIV (ritonavir-lopinavir) combination together with Ribavirin or Arbidol is under clinical trials. Favipiravir has been reported active against influenza virus, flavivirus and, foot and mouth disease virus. Both chloroquine and hydroxychloroquine were reported to inhibit both entry and post-entry stages of SARS-CoV-2. Besides the aforementioned drugs, other antiviral drugs may also be under clinical trial.

Cure of the disease (Vaccination)

According to latest reports [10], eight countries in the world have granted consent to vaccinate their people against the COVID-19 disease. Pfizer/BioNTech honoured the first in the world to discharge full late-stage trial data on November 18, 2020. On December 3, 2020 Britain became the first to authorize the shot for emergency use, accompanied by Canada and Food and Drug Administration (FDA) of the America on December 9 and December 11, 2020, respectively. Moderna honoured the second in the vaccine race on November 30, 2020 exhibiting a 94.1 per cent success rate for its vaccine. According to WHO's strategic advisory group of experts (SAGE), the Pfizer-BioNTech COVID-19 mRNA vaccine is secure and efficient [11].However people were advised to follow COVID-19 prevention measures. According to the report [11], a safeguarding effect begins to develop 12 days after the first dose. However, full safeguarding needs two doses to be administered with a 21 to 28-day time interval.

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