

A Review on Corona Virus: Biology and Pathophysiology

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Abstract

The Corona Virus Disease (COVID-19) is quickly spreading across China and globally. In this Review article we can study about Biology and Pathophysiology of Corona virus. How the disease can spread from China to Whole world. It became clear that the COVID-19 infection occurs through exposure to the virus, and both the immunosuppressed and normal population appear susceptible. Coronaviruses are enveloped single-stranded RNA viruses that are zoonotic in nature and cause symptoms ranging from those similar to the common cold to more severe respiratory, enteric, hepatic, and neurological symptoms.

Keywords: COVID-19; Biology; Pathophysiology; RNA virus

Introduction

What is the COVID-19 novel coronavirus?

The COVID-19, also known as the 2019 Novel Coronavirus, is a coronavirus like the Middle East Respiratory Syndrome (MERS) and SARS coronaviruses. However, it is distinct from SARS – this means that even if you have been exposed to SARS previously, you can still get the novel coronavirus.

Biology

- Coronaviruses are large, roughly spherical, particles with bulbous surface projections. The average diameter of the virus particles is around 125 nm (125 μm). The diameter of the envelope is 85 nm and the spikes are 20 nm long (Figure 1).
- The envelope of the virus in electron micrographs appears as a distinct pair of electron-dense shells (shells that are relatively opaque to the electron beam used to scan the virus particle).
- The viral envelope consists of a lipid bilayer, in which the membrane (M), envelope (E) and spike (S) structural proteins are anchored. The ratio of E:S:M in the lipid bilayer is approximately 1:20:300. On average a coronavirus particle has 74 surface spikes. A subset of coronaviruses (specifically the members of betacoronavirus subgroup A) also have a shorter spike-like surface protein called hemagglutinin esterase (HE).

- The coronavirus surface spikes are homotrimers of the S protein, which is composed of an S1 and S2 subunit. The homotrimeric S protein is a class I fusion protein which mediates the receptor binding and membrane fusion between the virus and host cell. The S1 subunit forms the head of the spike and has the receptor binding domain (RBD). The S2 subunit forms the stem which anchors the spike in the viral envelope and on protease activation enables fusion. The E and M protein are important in forming the viral envelope and maintaining its structural shape.
- Inside the envelope, there is the nucleocapsid, which is formed from multiple copies of the nucleocapsid (N) protein, which are bound to the positive-sense single-stranded RNA genome in a continuous beads-on-a-string type conformation. The lipid bilayer envelope, membrane proteins, and nucleocapsid protect the virus when it is outside the host cell.

Genome

Schematic representation of the genome organization and functional domains of S protein for SARS-CoV and MERS-CoV. Coronaviruses contain a positive-sense, single-stranded RNA genome. The genome size for coronaviruses ranges from 26.4 to 31.7 kilobases. The genome size is one of the largest among RNA viruses. The genome has a 5' methylated cap and a 3' polyadenylated tail.

The genome organization for a coronavirus is 5'-leader-UTR-replicase/transcriptase-spike (S)-envelope (E)-membrane (M)-nucleocapsid (N)-3'UTR-poly (A) tail. The open reading frames 1a and 1b, which occupy the first two-thirds of the genome, encode the replicase-transcriptase polyprotein (pp1ab). The replicase-transcriptase polyprotein self cleaves to form 16 nonstructural proteins (nsp1–nsp16).

The later reading frames encode the four major structural proteins: spike, envelope, membrane, and nucleocapsid. Interspersed between these reading frames are the reading frames for the accessory proteins.

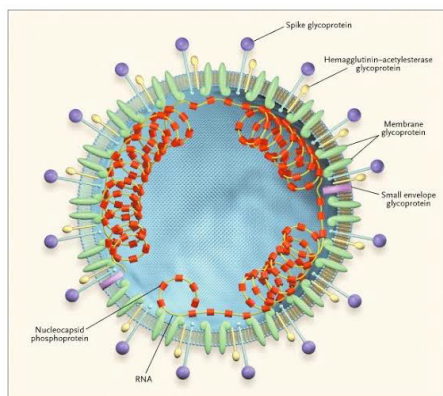


Figure 1: Cross-sectional model of a coronavirus.

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The number of accessory proteins and their function is unique depending on the specific coronavirus.

Replication Cycle

Entry

Infection begins when the viral spike protein attaches to its complementary host cell receptor. After attachment, a protease of the host cell cleaves and activates the receptor-attached spike protein. Depending on the host cell protease available, cleavage and activation allows the virus to enter the host cell by endocytosis or direct fusion of the viral envelop with the host membrane.

On entry into the host cell, the virus particle is uncoated, and its genome enters the cell cytoplasm. The coronavirus RNA genome has a 5' methylated cap and a 3' polyadenylated tail, which allows the RNA to attach to the host cell's ribosome for translation. The host ribosome translates the initial overlapping open reading frame of the virus genome and forms a long polyprotein. The polyprotein has its own proteases which cleave the polyprotein into multiple nonstructural proteins.

Replicase-Transcriptase Complex

A number of the nonstructural proteins coalesce to form a multi-protein Replicase-Transcriptase Complex (RTC). The main replicase-transcriptase protein is the RNA-dependent RNA polymerase (RdRp). It is directly involved in the replication and transcription of RNA from an RNA strand. The other nonstructural proteins in the complex assist in the replication and transcription process. The exoribonuclease nonstructural protein, for instance, provides extra fidelity to replication by providing a proofreading function which the RNA-dependent RNA polymerase lacks.

Replication

One of the main functions of the complex is to replicate the viral genome. RdRp directly mediates the synthesis of negative-sense genomic RNA from the positive-sense genomic RNA. This is followed by the replication of positive-sense genomic RNA from the negative-sense genomic RNA.

Transcription

The other important function of the complex is to transcribe the viral genome. RdRp directly mediates the synthesis of negative-sense subgenomic RNA molecules from the positive-sense genomic RNA. This process is followed by the transcription of these negative-sense subgenomic RNA molecules to their corresponding positive-sense mRNAs. The subgenomic mRNAs form a "nested set" which have a common 5'-head and partially duplicate 3'-end.

Recombination

The replicase-transcriptase complex is also capable of genetic recombination when at least two viral genomes are present in the same infected cell. RNA recombination appears to be a major driving force in determining genetic variability within a coronavirus species, the capability of a coronavirus species to jump from one host to another and, infrequently, in determining the emergence of novel coronaviruses. The exact mechanism of recombination in coronaviruses is unclear, but likely involves template switching during genome replication.

Release

The replicated positive-sense genomic RNA becomes the genome

of the progeny viruses. The mRNAs are gene transcripts of the last third of the virus genome after the initial overlapping reading frame. These mRNAs are translated by the host's ribosomes into the structural proteins and a number of accessory proteins. RNA translation occurs inside the endoplasmic reticulum. The viral structural proteins S, E, and M move along the secretory pathway into the Golgi intermediate compartment. There, the M proteins direct most protein-protein interactions required for assembly of viruses following its binding to the nucleocapsid. Progeny viruses are then released from the host cell by exocytosis through secretory vesicles. Once released the viruses can infect other host cells.

Transmission

Infected carriers are able to shed viruses into the environment. The interaction of the coronavirus spike protein with its complementary cell receptor is central in determining the tissue tropism, infectivity, and species range of the released virus. Coronaviruses mainly target epithelial cells. They are transmitted from one host to another host, depending on the coronavirus species, by either an aerosol, fomite, or fecal-oral route.

Human coronaviruses infect the epithelial cells of the respiratory tract, while animal coronaviruses generally infect the epithelial cells of the digestive tract. SARS coronavirus, for example, infects via an aerosol route, the human epithelial cells of the lungs by binding to the angiotensin-converting enzyme 2 (ACE2) receptor. Transmissible gastroenteritis coronavirus (TGEV) infects, via a fecal-oral route, the pig epithelial cells of the digestive tract by binding to the alanine aminopeptidase (APN) receptor.

Pathogenesis

- Coronaviruses are enveloped single-stranded RNA viruses that are zoonotic in nature and cause symptoms ranging from those similar to the common cold to more severe respiratory, enteric, hepatic, and neurological symptoms. Other than SARS-CoV-2, there are six known coronaviruses in humans: HCoV-229E, HCoV-OC43, SARS-CoV, HCoV-NL63, HCoV-HKU1, and MERS-CoV. Coronavirus has caused two large-scale pandemics in the last two decades: SARS and MERS [1].

- To detect the infection source of COVID-19, China CDC researchers collected 585 environmental samples from the Huanan Seafood Market in Wuhan, Hubei Province, China on 1 January and 12 January 2020. They detected 33 samples containing SARS-CoV-2 and indicated that it originated from wild animals sold in the market. Then, researchers used the lung fluid, blood, and throat swab samples of 15 patients to conduct laboratory tests. These laboratory tests found that the virus-specific nucleic acid sequences in the sample are different from those of known human coronavirus species.

- Laboratory results also indicated that SARSCoV-2 is similar to some of the beta (β) coronaviruses genera identified in bats, which is situated in a group of SARS/SARS-like CoV. To conduct next-generation sequencing from bronchoalveolar lavage fluid and cultured isolates, researchers enrolled nine inpatients in Wuhan with viral pneumonia and negative in common respiratory pathogens. The results of this next-generation sequencing indicated that SARS-CoV-2 was more distant from SARS-CoV (with about 79% sequence identity) and MERS-CoV (with about 50% sequence identity) than from two bat-derived SARS-like coronaviruses – bat-SL-CoVZC45 (with 87.9% sequence identity) and bat-SL-CoVZXC21 (with 87.2% sequence identity). Studies also reported that COVID-19 S-protein supported strong interaction with

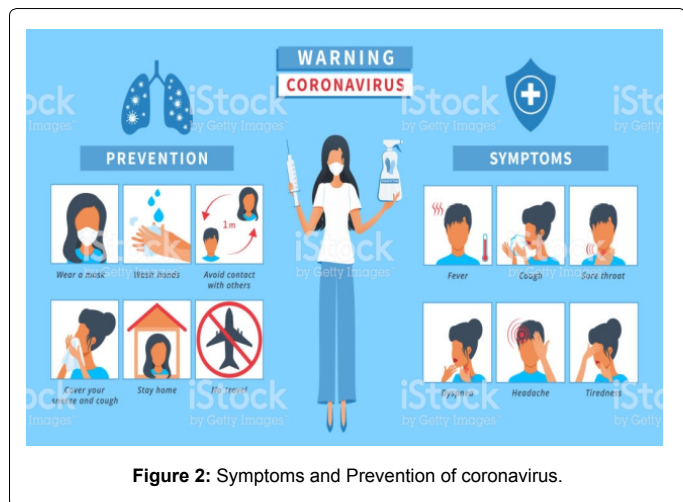


Figure 2: Symptoms and Prevention of coronavirus.

human ACE2 molecules despite the dissimilarity of its sequence with that of SARS-CoV.

The virus is not airborne. Virus transmission happens via droplets and contact [2].

Droplets: A person can get infected through the spit of an infected person landing on them.

Contact: A person can get infected through touching a surface (eg. a door handle or table) with infectious secretions (Figure 2).

Result

The Corona Virus Disease (COVID-19): Pathophysiology and Epidermology was studied.

Conclusion

Here we can conclude that Coronaviruses are enveloped single-stranded RNA viruses that are zoonotic in nature and cause symptoms ranging from those similar to the common cold to more severe respiratory, enteric, hepatic, and neurological symptoms.

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