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Mls 406 assignment

COVID-19(SARS-CoV-2)

COVID-19 is an acute respiratory disease caused by novel coronavirus SARS-CoV-2 also known as 2019-nCoV. On March11, 2020, the World Health Organization9WHO0 characterized COVID-19 as a pandemic. COVID-19 coronavirus SARS-CoV-2 belongs to the Betacoronavirus genus originating from bats. Betacoronaviruses can infect mammals, are zoonotic pathogens, and can cause severe respiratory disease in Humans. Other viruses in this family are SARS coronavirus and MERS coronavirus. COVID-19 has a similar receptor binding domain structure as SARS-CoV which suggests COVID-19 uses ACE2 receptor in humans for infection.

ETIOLOGY OF COVID-19

Coronavirus are positive-stranded RNA viruses with a crown-like appearance under an electron microscope due to the presence of spike glycoproteins on the envelope. The subfamily Orthocoronavirinae of the Coronaviridae family(order Nidovirales)classifies into four genera of Coronavirus: Alphcoronavirus, Betacoronavirus, Deltacoronavirus, Gammacoronavirus and furthermore, the betacoronavirus genus divides into five sub-genera or lineages. Genomic characterization has shown that probably bats and rodents are the gene sources of alpha and betacoronavirus. On the contrary, avian species seem to represent the gene sources of delta and gammacoronavirus.

Members of this large family of viruses can cause respiratory, enteric, hepatic, and neurological diseases in different animal species, including camels, cattle, cats, and bats. Seven human coronaviruses are capable of infecting humans have been identified. Some of HCoVs were identified in the mid-1960s, while others were only detected in the new millennium.

.Common HCoVs: HCoV-OC43, and HCoV-HKU1(betaCoVs of the A lineage);HCoV-229E, and HCoV-NL63 (alphaCoVs).They can cause common cold and self-limiting upper respiratory infections in immunocompetent individuals. In immunocompromised subjects and the elderly, lower respiratory tract infection can occur.

.Other HCoVs: SARS-CoV, SARS-CoV-2, and MERS-CoV (betaCoVs of the B and C lineage, respectively). This cause epidemics with variable clinical severity featuring respiratory and extra-respiratory manifestations.

Thus SARS-CoV-2 belongs to the betaCoVs category. It has round or elliptic and often pleomorphic form, and a diameter of approximately 60-140nm. Like other CoVs, it is sensitive to ultraviolet rays and heat. These viruses can be effectively inactivated by lipid solvents including ether(75%), ethanol, chlorine-containing disinfectant,chloroform except for chlorhexidine.

ORIGIN OF COVID-19

Recently at the end of 2019, wuhan an emerging business hub of china experienced an outbreak of novel coronavirus that killed more than eighteen hundred and infected over seventy thousand individuals within the first fifty days of epidemic. This virus was reported to be the beta group of coronaviruses. The novel virus was named as Wuhan coronavirus or 2019 novel coronavirus(2019-nCov) by the chinese researchers. The international committee on Taxonomy of viruses(ICTV) named the virus as SARS-CoV -2and the disease as COVID-19.

It was found that the genome sequence of SARS-CoV-2 is 96.2% identical to a bat CoV RaTG13, whereas it shares 79.5% identity to SARS-CoV. Based on virus genome sequencing results and evolutionary analysis, bat have been suspected as natural host of virus origin, and SARS-CoV-2 might be transmitted from bats via unknown intermediate hosts to infect humans. It is clear now that SARS-CoV-2 could use angiotensin-converting enzyme 2 (ACE2), the same receptor as SARS-CoV to infect humans.

STRUCTURE OF COVID-19

The structure of COVID-19 consist of the following:

-A spike protein (S) -Hemagglutinin-esterease dimer (HE) -A membrane glycoprotein (M) -An envelope protein (E) -A nucleocapsid protein (N) -And RNA

SPIKE PROTEIN: It is heavily glycosylated, utilizes an N-terminal signal sequence to gain access to the ER and mediate attachment to host receptors. It is the largest structure and makes the distinct spikes on the surface of the virus. For most coronaviruses, S protein is cleaved by a host cell furin-like protease into two separate polypeptides S1 and S2.

RNA: Is the genome of the virus.

NUCLEOCAPSID PROTEIN: Binds to RNA in vitro and is heavily phosphorylated. N proteins binds to viral genome in a beads on a string type conformation. This protein likely helps tether the viral genome to replicase-transcriptase complex, and subsequently package the encapsulated genome into viral particles.

ENVELOPE PROTEIN: Is found in small quantity in within the virus. It is most likely a transmembrane protein and with ion channel activity. The protein facilitates assembly and release of the virus and has other functions such as ion channel activity. It is not necessary for viral replication but it is for pathogenesis.

MEMBRANE PROTEIN: Is the most abundant structural protein. It does not contain signal sequence and exist as a dimer in the virion. It may have two different conformations to enable it to promote membrane curvature as well as bind to nucleocapsid.

HEMAGGLUTININ-ESTERASE DIMER PROTEIN: Is present in a subset of betacoronaviruses. The protein binds sialic acids on surface glycoproteins. The protein activities are thought to enhance S protein-mediated cell entry and virus spread through the mucosa.

PATHOPHYSIOLOGY OF COVID-19

CoVs are enveloped, positive-stranded RNA viruses with nucleocapsid. For addressing pathogenetic mechanisms of SARS-CoV-2, Its viral structure, and genome must be considerations. In CoVs, the genomic structure is organized in a +ssRNA of approximately 30kb in length- the largest known RNA viruses – and with 5’-cap structure and 3’0poly-A tail. Starting from the viral RNA, the synthesis of polyprotein 1a/1ab (pp1a/pp1ab) in the host is realized. The transcription works through the replication –transcription complex organized in double-membrane vesicles and via the synthesis of subgenomic mRNAs (sgRNAs) sequences. Note that transcription termination occurs at transcription regulatory sequences, located within the so called open reading frames (ORFs)that work was templates for the production of subgenomic mRNAs. In the atypical CoV genome, at least 6 ORFs can be present. Among these, a frame shift between ORF1a and ORF1b guides the production of both pp1a and pp1ab polypeptides that are processed by virally encoded chymotrypsin-like protease (3CLpro) or main protease (Mpro), as well as one or two papain-like proteases for producing 16 non-structural proteins (nsps). Apart from ORF1a and ORF1b, other ORFs encode for structural proteins, including spike, membrane, envelope, and nucleocapsid proteins.

Pathophysiology and virulence mechanisms of coronavirus and therefore also of SARS-CoV-2 have links to the function of the nsps and structural proteins. For instance, research underlined that nsp is able to block the host innate immunue response. Among functions of structural proteins, the envelope has a crucial role in virus pathogenicity as it promotes viral assembly and release .

References

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