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Biochemistry of Corona Virus Infections: A review article

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Abstract: By the end of 2019, a new virus called Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-CoV-2), which was at the time causing a serious respiratory syndrome, grew rapidly starting from Wuhan in China. Around March 2020, the world's Apex health organization, World Health Organization (WHO), stated that it was a global pandemic. In this review, we attempt to summarize the medical characteristics information regarding the novel virus's prevention, tests, and treatments. The data used for this review were gathered from various academic research reports and publications, WHO publications, etc. However, the readers of this review must be informed that there are continually new reports on this virus as more studies are undertaken by various professional bodies. All over the world, this disease has caused various extents of illness with varying symptoms such as fever, cough, fatigue, etc. It is reported that it can be treated via symptomatic treatment, antiviral drugs, and oxygen therapy. To prevent the rapid

transmission of this virus, it is imperative to identify potential cases as soon as possible and isolate them from the unsuspecting populace

Keywords—coronavirus; severe acute respiratory syndrome; translation; genome replication; transcription

1. INTRODUCTION

Coronaviruses (CoVs) are known to have been the cause of the worldwide severe acute respiratory syndrome (SARS) outbreak in 2003 and resulted in a devastating cause of over 8,000 infections. This was reported to result in a severe fatality rate of approximately 10%. CoVs are enteric diseases in livestock, animals and even human beings. They are known to possess the most complex and largest positive-stranded RNA genome [1, 2]. Strikingly, they have also been suggested to have numerous RNA processing enzymes that are not similar to small RNA viruses [3].

For more than 20 years, three CoVs have, from time to time, crossed animal species, including bats, transmitted to human beings and resulted in a huge-scale disease outbreak. These include SARS-CoV and also middle east respiratory syndrome (MERS) CoV, which have been found to cause adverse respiratory diseases in human beings [4]. SARS-CoV-2 is a new CoV and causes COVID-19. It is known to have spread fast worldwide since it was first recorded in Wuhan, China, in the latter part of 2019. Studies revealed that it is a severe disease with a 2% mortality rate.

Surprisingly, this new virus has been noted to give mild to serious respiratory diseases in humans. It has the power of moving from one species to another and causing a wide range of diseases as an unfamiliar and complex pathogen [5]. A lot of morphological and biochemical changes occur in a CoV- infected cell. Studies have revealed that infection by varying CoVs can cause changes in the translation and transcription patterns, cytoskeleton, and also cell cycle. More so, CoV infection can alter the immune and stress responses of a host, cause inflammation and even change coagulation pathways.

Advances in the study of CoVs effects in a host have been recorded with the mouse hepatitis virus (MHV) system and, most recently, with the SARS-CoV [6-8].

2. COVS STRUCTURES

CoVs are known to be part of the Nidovirales order and Corona viridae family. This family consists of two smaller families, namely Orthocoronavirinae and Letovirinae [9]. Genotypically, CoVs are grouped into four genera which are alpha (α), beta (β), gamma (γ), and delta. β-CoV is sub grouped into four viral lineages of A-D. CoV is an envelope but also a virus which is unsegmented, and has a big positive-sense single-stranded RNA virus genome. It is also known to be poly-adenylated and capped [10]. They are known for their crown-shape spikes which protrudes out of their surfaces, hence their name was derived from this fact. The CoV spike (S) glycoprotein is attached to cellular receptors on cell of their host and mediates viral entry which results in inter-species pathogenesis and transmission [11].

The RNA genome of the new corona virus-2019 (nCoV-2019) has 29891 nucleotides in length, and encodes 9860 amino acids [12]. nCoV-2019 genome components include: two flanking untranslated regions (UTRs); a single open reading frame (ORF1ab) (7096-aa); a polyprotein (7096-aa); structural proteins (which include a spike (S), an envelope (E), a membrane (M), and a nucleocapsid (N); and five accessory proteins [4].

Recent studies on the physico-chemical characteristics of nCoV-2019 revealed that when exposed to a temperature of 56 oC for 30 minutes using an ultraviolet radiation, it can be inactivated. Also, it can be inactivated by using a lipid solvent (for example, 75% ethanol), chloroform and disinfectants which contain chlorine. Of over 30 known CoVs which can infect human beings, and mammals, α- and β-CoVs are the only ones known to be zoonotic in origin [13]. Human α-CoVs (which include NL63, 229E, OC43, and HKU1), usually cause mild respiratory infection in patients whose immune systems are uncompromised, and can be seen having symptoms such as fever, headache, etc. Human β-CoVs include SARS-CoV and MERS-CoV. They have no sign or symptom in the early or primary stage. However, they can rapidly progress to intense pneumonia and even death. The mortality rate is about 10 % and 35 % in patients who are immuno-competent and immuno- compromised respectively [14]. Amazingly, virus genome sequence analysis of COVID-19 have revealed a 96.2 % similarity with Bat CoV RaTG13. This suggests that SARS-CoV-2 and bat CoV might have a common origin [15].

2.1 Clinical Symptoms of Covid-19 Diseases

For most patients, the common clinical symptoms are fever, dry cough and shortness of breath. Some also have sore throat, headache, diarrhea and fatigue

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[16]. Patients with mild pneumonia do not mostly show any severe symptoms or even complications, while patients with serious pneumonia usually experience acute respiratory distress syndrome (ARDS) and refractory hypoxaemia.

nCoV-2019 can result in serious pulmonary infection, failure of the respiratory system along side organ damage and malfunction. Studies have also revealed that the disease is mild in most of the patients and only a little portion develop serious pneumonia, pulmonary edema or various organ damages.

The infection usually shows much milder clinical symptoms or none in children when compared with adults. SARS-CoV-2 is known to have a higher probability of affecting older persons with severe disease because of their poorer immune system.

The disease has been noted to infect more males than females [17]. This lesser tendency of viral infection in females when compare with males can be closely related to the protective power of the X chromosome and sex hormones [18].

2.2 CRISPR/Cas13: A Fast Method for COVID-19 Detection and Treatment

CRISPR-Cas13-based SHERLOCK system comprises two RNA guides. These guides are Cash 13 protein and they form a SHERLOCK system which helps to note the presence of COVID-19 RNA. At first, fragment of SARS-CoV-2 RNA which is synthetic in nature is used as a pattern for designing two RNA guides, which have the capacity of binding to their complementary sequences in COVID-19 RNA. In order to help this to be read visually, a paper strip is used and it is dipped into a prepared sample. If a line appears on the paper strip, the presence of a virus is indicated in the sample.

Another research group have also suggested a RNA- targeting CRISPR system which targets the RNA genome of SARS-CoV-2 in the laboratory. This system is a new technique and is applicable for the treatment of all the various kinds of RNA virus infections. This technique is very useful because of its capacity to target different virus variants that evolve and have tee tendency to escape traditional drugs [19].

3. Molecular Mechanism of COVID-19

SARS-CoV-2 is recorded to have a higher binding affinity to human beings than SARS-CoV. Hence, this explains why there are more cases of the former than the later.

Immediately the virus enters the host, the viral RNA is released into the cytoplasm of the host. It goes on to translate itself into two poly proteins and structural proteins which are quickly followed by a replication of the viral genome. Thereafter, the fresh envelope glycoproteins which are formed enters the endoplasmic reticulum (ER). The virus buds sprout into the ER- golgi intermediate chamber. Finally, the vesicles containing the virus particles blend with the plasma membrane and this discharges the virus [20].

3.1 Pathophysiology of COVID-19

Genomic studies have shown that CoVs have the most abundant RNA genome, a 5'- capping site and a 3' poly-A tail region which help to improve the host genome transcription and translation. The virus is generally grouped into four categories which are alpha, beta, gamma and delta. This categorization is based on the genomic structure as traget host. In the host genome, the pathogenic in vivo appearance of the virus falls into various stages, which are; the binding of the virus to the host receptors; the entrance of the virus into the host cells by membrane fusion or by endocytosis; the release of the virus particles within the host cell (which is followed by the replication and the biosynthesis of viral proteins); and the budding of viral particles. Human SARS-CoV-2 and SARS-CoV are identical (82% identical) in the work of non-structural proteins (nsps) and structural proteins (sps) when comparing their pathophysiology and virulence mechanism. CoV genome has six open reading frames (ORFs), of which ORF1a and ORF1b encode 16 naps which are typically crucial for virus transcription and replication.

3.2 Influence of Viral and Cellular Proteins on CoV Replication

The replication of CoV uses compound mechanisms that include viral and cellular proteins. The replication occurs in the cytoplasm in a membrane- protected micro environment which contains all the protein functions needed for viral RNA synthesis. The studies of MHV- infected cells via electron microscope have revealed that these structures consist of double- membrane vesicles (DMVs) that are likely generated via the use of cellular autophagy- related processes. Structures which are

identical to DMVs have been seen in SARS-CoV and in the equine arteritis virus (EAV) infection, which uggests that CoV and arteritis virus have a similar replication strategy. It is known that CoV replication occurs within the cytoplasm. However, CoVs can control the cell machinery by locating some of their proteins in the host cell nucleus. Till date, two CoV proteins and another two from arteritis viruses have been cited in the nucleolus of infected cells. During infection, viruses interact with nucleolar antigens and this leads to their redistribution [21].

3.3 CoV Translation

Genomes of positive- strand RNA viruses, consist of an m7GpppN- cap structure at the 5- end of the mRNA and are thought to start the translation process in a cap- dependent manner. CoV mRNAs have a polycistronic configuration, with the exception of mRNA which is encoded by the most 3- end of the genome. However, there is evidence which shows that some of the CoV mRNAs are bicistronic or even tricistronic. Translation can be regulated by viral or cellular factors acting in trans- or by cis- elements within the 5UTR [22].

3.4 CoV Genome Replication and Transcription

CoV replication and transcription usually need the recognition of RNA genome 5 and 3- ends by cellular and viral proteins. CoV genome replication is done via the synthesis of RNA, which is a negative strand. Later on, this becomes the template for synthesizing progeny virus genomes. Via mapping studies using MHV defective-interfering (DI) RNAs, it has been noted that 470 nt from the 5- end and 436 nt from the 3- end are required for the DI RNA replication. The 3- end of the genome is the last region reached by the viral polymerase during the synthesis of the positive strand. Thus, it is noted that the replication signal at the 3- end of the genome may interact with signals at the 5- end to exert its effect on RNA synthesis.

N protein is noted to have an important role in CoV replication and transcription because it hugely influences many viral and cellular processes. For some time, the debate has been ongoing about the requirement of N protein for virus replication and transcription.

CoV transcription depends on RNA synthesis and involves steps that are not continuous during sg mRNAs production. This process usually produces a nested set of sg mRNAs which are 5- and 3- coterminal with the virus genome [23, 24].

4. TREATMENT OPTIONS

4. ANTI-VIRUS THERAPY

There are drug therapies known to be approved for treating deadly infectious diseases such as Ebola, AIDS, etc. These therapies are also beneficial in treating COVID-19. However, it is imperative to note that other therapeutic methods still can not be used. These include the use of corticosteroids for viral therapy. In combination with chloroquine, hydroxychloroquine and ritonavir have also been proposed as one of the drug therapies for the treatment of COVID-19.

4.1 Improvement of the Immune System

The immune system can be improved to fight the virus. Usually, when there is a viral infection, the duplicating virus is destroyed by antiviral immune responses, leading to the fast removal of the virus. When the CoV enters the host, it infects the macrophages. This it does by sticking itself to the DPP4 on the host cell via the help of the spike proteins, which could consequently lead to the release of genomic RNA in the cytoplasm. The macrophages give the CoV antigens to the T- cells, which play a key role in the antiviral immune system. After that, the T-cell is activated and differentiated by the antigen presented, and this leads to the production of large release of huge amounts of cytokines for the reinforcement of the immune response. CoVs induce the production of the mediators that negatively affect the activation of NK and CD8 T- cells. Amazingly, the CD8 T- cells keep on producing huge quantities of cytokines to remove CoVs. During CoVs infection, the virus- host interaction causes the production of immune mediators that result in the elevated secretion of chemokines and cytokines. This high amount of chemokines and cytokines aids in the recruitment of lymphocytes and leukocytes at the viral infection site for the removal of the virus. Therefore, targeted immunotherapy is a good and appropriate alternative to some antiviral drugs which have a low therapeutic effect or in persons who have been known to show resistance to drugs [25].

4.2 Vitamins

Studies have proved that vitamins are vital in clinical therapies. Vitamin D is known to help improve the immunity of the cells by decreasing the cytokine storm in COVID-19. This they do by causing pro and anti-inflammatory factors. Many studies have

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suggested that vitamin D capsules can decrease the risk and seriousness of COVID-19.

4.3 Other Treatments

Although various studies have stated that Western medicines can be used to treat COVID-19, Chinese traditional medicine has also shown a promising effect on the treatment of COVID-19. According to research, patients suffering from SARS or MERS have similar treatment plans. In China, both traditional Chinese and Western medicines can be used to treat COVID-19. Some of these traditional Chinese medicines include herbal folk therapies and herbal teas. However, it is important to state that studies have also suggested that some traditional medicines might not be good for human consumption. The

In India, the Ministry of AYUSH has stated that herbal medicines could be useful in fighting the outbreak of CoV and also aid in reducing its infections. The Central Council for Ayurvedic Sciences Research (CCRAS), an autonomous body of AYUSH, produced Ayush-64, which is recorded to be a good treatment for patients suffering from CoV. More so, some anti-inflammatory ayurvedic drugs have also been used to treat CoV because they improve immunity [20].

5. CONCLUSION

There is a lot to learn about how CoV behaves in human beings. However, quickly identifying this new virus will aid in properly examining antiviral compounds and developing more vaccines. This paper reviewed the information on genome sequences, protein structures and how the virus functions. We tried to ascertain the evolutionary trajectories and virus-host interactions, which will aid virologists in deepening their knowledge of the topic. We must note that a better knowledge of probable molecular mechanisms behind CoV infection and the pathogenesis of SARS-CoV-2- related pneumonia will assist in developing more antiviral drugs and vaccines, which would help decrease the mortality rate of this virus in the nearest future.

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