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Review Article

A Review on Key Modulatory Novel Features, Viral Assembly, Biomarkers Associated with Biological Replication and Molecular Genetics in Progression of Coronaviruses

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Abstract

There are many viruses that cause different infectious diseases in human as well as in vertebrate systems of different animals. Coronaviruses are the most infectious viruses belonging to the family *Coronaviridae*. The genome of coronaviruses are made up of RNA and size about the ~30 kb that contain the 5′ cap structure along with a 3′ poly (A) tail. These are helpful for translating the different proteins causing infections such as replicase proteins. Different types of immune based responses evoked once the viral attack on the immune cells of the body. Accessory proteins also playing important role as inflammatory responses once viral attack on immune cells and release of different inflammatory genes that are involved in progression of COVID-19. One of such kind of response from interferon's I and III are cytokines that playing important role against the viral infections. Lopinavir and Ritonavir both inhibiting the viral replication and translation by targeting the viral relapse and other necessary genes involved in viral genome. Dexamethasone, may help manage symptoms in people with COVID-19 by reducing inflammation. Vaccines and different therapeutics medicines are employed to damage the structure of virion and nucleocapsid by underlying the cellular mechanism of COVID-19.

Keywords: COVID-19, Inflammation, Gene markers, biochemical response, gene activation.

INTRODUCTION

There are many viruses that cause infectious diseases in human as well as vertebrates systems of different animals [1]. The major root cause of infectious diseases is the replicating body of viruses that attack on the host by using their metabolic machinery. In this way, viruses are most leading causing of deaths due the widespread infections all around the world. Coronaviruses are most infectious viruses belonging to the in the family *Coronaviridae* and remain a cause of many deaths in 2019. Based on its phylogenetic relationships and genomic structures the COVID-19 belongs to genera Beta coronavirus which has a close similarity of the sequences of COVID19 to that of severe acute respiratory syndrome-related coronaviruses[2, 3]. There is need to control the COVID-19 as it is the most deadly virus that causes lungs cells to inflamed and patients in this diseases difficult to breathe due to more colonization of virus in alveolar wall and bronchi[1].

Different drugs are formulated for controlling the prevalence of COVID-19. As these viruses have high infections rate as compared to the other viruses so the drugs with high antiviral effects can be used [4]. Coronavirus, the RNA polymerase of the viruses is an established target for inhibiting the viral replication and has pre-established values for clinical engagements by the broad-spectrum nucleotides, such as prod drug remdesivir. There are many other therapeutics and ongoing experiments in combating the COVID-19. The main goal is to control the COVID-19 with minimal effects of drugs used to take the viral proteins [5, 6].

Table-1: Shows the various features of coronaviruses family and target genes

Biological Features	Proteins/Techniques	Assembly /Target	[Reference]
Structural Features	cryo-electron tomography	125 nm as depicted and shape usually spherical with spike projections emanating from the surface of the virions	[16,17]
Replication Factors	Replicase-transcriptase	Cellular and molecular assembly	[9,10]
Antiviral drugs	For breaking the cellular machinery of replicase genes	Cellular and molecular assembly	[13,14,15]
Immune responses	Interferon's ,interleukin	Cellular and molecular assembly	[18,19]
Dexamethasone	corticosteroids	For targeting the COVID-19	[28,29,30]

Biological Features of Replication and associated proteins

There are different aspects of replicating of coronavirus in the host and tract the different tissues. The transcription begins with the help of replicase-transcriptase together with other viral proteins and, possibly, cellular proteins, assemble into membrane-bound replication-transcription complexes [7, 8]. This complex making essential role in reminting the virus into the host by damaging its cellular structure. These main types of complexes assembled at the at perinuclear regions and are associated with double-membrane vesicles [9, 10].

The genome of coronavirus are the made up of RNA and size about the ~30 kb that contain the 5′ cap structure along with a 3′ poly (A) tail. These helpful for translating the different proteins causing infections such as replicase proteins. Different genes are expressed during replicating of coronavirus. Their high expression leads to increases the chances of viral attack to the body cells. Low expression helps to control the viral proteins target by different drugs and antiviral therapeutics [11, 12]. The most important gens are replicase gene encoding the non-structural proteins. These genes are making the genomic parts of the coronavirus as it has large genome size. Different drugs are used for breaking the cellular machinery of replicase genes but mechanism remains unclear due to more loads of viruses in the repository duct and blockage of mucous. It leads to dysfunction of cellular functions of lungs with extensive treatment need after the attack of COVID-19[13-15].

The complex structure the coronavirus visions have been studied through different experimental techniques such as cryo-electron tomography, cryo-electron microscopy and revealing its structural features such as diameter 125 nm as depicted and shape usually spherical with spike projections emanating from the surface of the virions. These structures are involving in making the complex machinery of coronavirus with active metabolic machinery inside the host cells. Vaccines and different therapeutics medicines are employed to damage the structure of virion and nucleocapsid by underlying the cellular mechanism of COVID-19[16, 17].

There are different types of immune based responses once the viral attack on the immune cells of the body. One of such kind of response from Interferons I and III are cytokines that playing important role against the viral infections. These cytokines are released once virus attacks by thereby triggering the Jak-Stat (Janus kinase/signal transducer and activator of transcription) signaling pathway that switches on many antiviral genes. The activated interferon's stimulated the different genes that suppress down the viral replication and inhibitions of viral RNA into the translation processes. Thus, interferon's as biomarkers indicating the cellular infections caused by viruses, helpful for controlling the metabolic machinery of viruses and overall can target the viral genes to be suppress through activation of suppressor genes [18, 19].

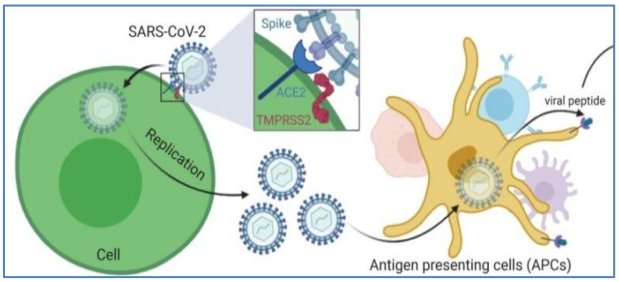

Fig-1: Shows the markers involved in replication of SARS-COV-2

Different studies showed that biomarkers are involved for early detection and diagnosis of inflammatory proteins in COVID-19 such as interleukin 6 (IL-6), tumor necrosis factor alpha (TNF-α) and interferon gamma (IFN-γ). These inflammatory markers hive levels in blood indicating that severe of disease progression. Accessory proteins also playing important role as inflammatory responses once viral attack on immune cells and release of different inflammatory genes that are involved in progression of COVID-19 [20-22]. The accessory proteins in coronaviruses vary in number, location and size in the different viral subgroups, and are thought to contain additional functions that are often not required for virus replication, but are involved in pathogenicity. There is need to design such kings of drugs that show friendly interaction with the viral particles in order to target them effectively and then blocking the viral replication, translation [23].

Table-2: Shows the different principle techniques used for detection of coronaviruses

Technique	Principle Follow up	Advantages	Reference
PCR	Molecular	PCR is the become the prominent technique for detecting the , viral pathogens, toxins, corona viruses family due to specific amplification of the nuclear region	[10,11,20]
RT-PCR	Molecular	Real time PCR is the most advanced form that helpful for detection the nucleic acid testing in short time with greater chances of accuracy as compared to the other kit based traditional methods for detection of nuclear segments	[12,27]
ELISA	Clinical	ELISA is used in both experimental and diagnostic virology. It is used for detection of infections by many different viruses, including HIV-1, HTLV-1, adenovirus, and cytomegalovirus	[1,4,8,9]
Other techniques	Molecular	Loop-mediated isothermal amplification (LAMP) is used for viral detection through nucleic acid testing with high accuracy and has become popular technique during pandemic of Covid-19.	[14,18, 28]

Different combinations of medicines and antibodies are employed in order to control the viral load. Traditional medicines as emerging option in controlling the COVID-19 as it has been major source of medications for controlling the different diseases such as malaria. The contribution of traditional medicine in the management of Covid-19 may complement healthcare prevention and medical care services [23, 24]. There are different opinions of different scientist about the traditional medicines as these are not reliable in targeting the viral proteins and poor responses in response of virus's entry into the host. While on the other hand, advances in pharmacology leads to innovations of different drugs by relaxing the traditional drugs as traditional drugs not helpful for overall diseases treating. Modern technologies leads synthesized the drugs for controlling the viral infections but chemicals formulations leads to increase chances of metastasis probably with compromised immune system. There are ceresin medical risks of potentially relevant additional risk factors are prolonged isolation, use of experimental medical treatments associated with neuropsychiatric side effects (e.g. antimalarial and antiviral drugs), prolonged mechanical ventilation and acute renal impairment. The long term medical therapy with inductions of chemicals leads to different borne of different disorders and difficult to treat at early stage [25].

Different Drugs and their action on human body

There are different drugs used to treat the COVID-19 but some of them are ineffective in controlling the viral infections and active replication rate. The most potential drugs used to treatment of COVID-19 are lopinavir and ritonavir that can tightly attack on polypeptide chains of CIVID-19 by cleaving long polypeptides chains during the assembly of new viruses. Lopinavir and Ritonavir both inhibiting the viral replication and translation by targeting the viral relapse and other necessary gens involved in viral genome. Thus, lopinavir and ritonavir posing a possible potent therapeutic option against SARS-CoV-2. There is another drug that inhibiting the viral proteins to replicate is the Ivermectin, a popular anti-parasitic drug, acts on SARS-CoV-2 by preventing viral proteins from entering the host cell nucleus. These potential drugs are most promising in combating the replication and translations processes of infectious viruses [25-27].

Different corticosteroids also used to reduce the inflammation rate caused by COVID-19. One of such kind of corticosteroids, dexamethasone, may help manage symptoms in people with COVID-19 by reducing inflammation. It may helpful for control the

deaths especially COVID-19 by reducing the inflammation all around the world. COVID-19 therapies are useful but some of them with effective chemical treatments leads to cellular toxicity and death of cells. There is need to design the effective drugs that should be safe and mode of action on cells with side effects at all that may reducing the morbidly rate all around the world[28-30].

CONCLUSION

There are many viruses that cause different diseases in human but most replicating one is COVID-19 that causes the respiratory tract to bock and thus causing the severe infections in lungs. Due to which, air cannot flow into lungs, as a result, chances of deaths increases. There is need to design the biomedical therapy and effective vaccines that can be control the viral target proteins. Medical therapies also available, but effective one needed in order to combat this infection caused by coronaviruses.

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