

Novel corona virus and its druggable targets

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Abstract

Novel corona virus or Covid-19 is a single stranded RNA virus. It is the part of the corona virus family. The latest pandemic covid-19 is caused by the novel corona virus. The symptoms of novel corona virus infection are varying from mild to chronic. The specific and effective treatment of the novel corona virus is not available yet.

Since SARS-CoV and MERS-CoV are also part of the corona virus family and it is similar to novel corona virus, so we can identify the drug target by studying them.

Novel Corona virus has some essential structural proteins like spikes, envelop, membrane and nucleocapsid proteins, hence we can target that proteins by drugs.

In SARS-CoV, most important protein for the host cell attachments and fusion into the host cells is spikes proteins (same as of in novel corona virus). Therefore it is potential target for the development of anti-corona drugs. Including the spikes proteins, other prominent targets of novel corona virus are haemagglutinin esterase, helicase and protease.

On the other hand, utilizing the knowledge and therapy of the alternative medicinal systems like ayurvedic and homeopathic may provide better alternative for the treatment of novel corona virus/covid-19.

Keywords: Novel corona virus, Covid-19, SARS-CoV, MERS-CoV, Spikes proteins, Anti-corona drugs targets.

Introduction

Novel Coronavirus or Covid-19 belongs to the coronavirus family, which cause infectious disease to the mammals and birds.¹ Coronaviruses are transmitted between the animals and humans, so it is zoonotic in nature.

Viruses of coronavirus family are single stranded RNA viruses. And their genome size ranges from 27-34 kilobases (kb). And they are largest among the RNA viruses. They are enveloped viruses and having the positive-sense single stranded RNA genome.² They have a nucleocapsid of helical symmetry. And their surfaces are covered by club-shaped protein spikes.

Early incidences of coronavirus infections were SARS-CoV and MERS-CoV. It was reported that SARS-CoV was transmitted from civet cats and MERS-CoV transmitted from dromedary camels to the humans.³ Several other viruses of the coronavirus family are known in animal infections and diseases but they have not infected or transmitted to the humans yet.

Recently reported novel corona virus was first identified and outbreak in Wuhan, China. And it has not been reported before.

Symptoms

Common signs and symptoms of Novel corona virus (covid-19) are, cough, fever, shortness of breath, breathing difficulties in mild conditions.⁴ And pneumonia, severe acute respiratory syndromes, kidney failure and even death in the severe conditions.

Treatments

There is no any breakthrough has been reported yet to treat the Covid-19. And also there are no any vaccines are available in the markets. But the studies are ongoing to report the promising treatment of it.

According to situations and knowledge, various countries and doctors use the drug repurposing approach to treat Covid-19. They have used the potential antiviral drugs to anti-malarial drugs like, chloroquine, darunavir, galidesivir, lopinavir/ritonavir combination, remdesivir, triazavirin, Umifenovir and darunavir.⁵ Many doctors and researchers also use the plasma therapy and interferon beta.

Novel Corona Virus

To harness the Covid-19, it has required to identifying the drug targets of novel corona virus (covid-19). For the

successful identification the drug target and drugging it, thorough knowledge of structure, life cycle, maturation cycle and metabolic pathways of the novel corona virus and other viruses of this family has been required.⁶

Since the complete details of the Covid-19 is not available yet. And early epidemic SARS and MERS were also belongs to same virus family and similar to that of Covid-19, so we have taken the SARS and MERS as references to study the possible drug targets and the treatment of Covid-19.

The various structural proteins like spikes, envelop, membrane and nucleocapsid proteins are produced by the mRNA. This mRNA is produced by the specific part of the novel corona virus's genome.⁷ Other potential envelop-associated protein is haemagglutinin esterase glycoprotein or HE protein, which is present in some of the corona viruses of corona virus family.^{8,9}

SARS (Severe Acute Respiratory Syndrome) is an acute respiratory diseases condition caused by the SARS-CoV virus. SARS-CoV virus is an etiological agent and it is zoonosis of a highly related animal coronavirus. The SARs epidemic was reported in the winter 2002-2003.¹⁰

Spikes Proteins and Possible Targets

The characteristic spike proteins (as in the Covid-19) of SARS-CoV virus are responsible for the infection and binding with receptor bearing cells. For the infection, the binding of the SARS-CoV virus with its receptor present on the human/animal cells is mandatory (same in the case of Covid-19).¹¹ In the humans, Angiotension Converting Enzyme 2 (ACE 2) is the cellular receptor for the SARS-CoV.¹²

Spikes glycoprotein of the SARS-CoV bind with the ACE 2 receptors and got entered into the host cells.¹³ The spikes proteins belongs to the class I viral fusion proteins.

Process of SARS-CoV fusion/entry into the host cells is as follow:

It consist of 3 steps process, (1) Binding with the receptors present on the cells, receptor binding initiates the conformational changes in the Spikes glycoproteins. (2) Proteolysis (3) Activation of the membrane fusion within the endosomes.

After the virus-cell attachments, virus enters into the cells by extensive refolding process which involves the formation of a coiled structure, and ultimately fused into the target cells membrane. Hence, variation in the activity of the cellular proteases can modulate the

efficiency of the entry of the viruses into the ACE-2 bearing cells.

As we have discussed the spikes proteins are fusion proteins. So in the virus producing cells, spikes proteins cleaved into two sub-units S1 (receptor binding unit) and S2 (c-terminal membrane-anchored fusion unit) by furin-like protease (as in the case of other class 1 fusion proteins like filoviruses, marburgviruses, influenza viruses, HIV-1 and ebola).

SARS-CoV spike proteins and other pseudo typed retroviruses utilized the enzymatic activity of the endosomal proteases for the virus entry. This suggests the possibility that, during the cells entry it has required the proteolytic activation of the spikes proteins in the endosomal route. This suggests the possibility of proteolytic activation of the spike protein in the endosomal route during cell entry rather than during cell exit.³

Spike proteins are indispensable for the virus entry into the cell and for the infection, therefore it is the important target for the drugs of novel corona virus. Apart from spikes proteins, other potential drug targets of corona virus family and novel corona virus are haemagglutinin esterase, helicase and protease.¹

Conclusion

Novel corona virus or Covid-19 is a novel virus of the corona virus family. It is more infectious in nature than deadlier/lethal.

For the management of the covid-19 medical emergency of the world, it has required the rational research and study. Numbers of researchers and pharmaceutical companies are trying to develop the drugs and vaccines to get rid of it.

The first step in the infection of novel corona virus is its entry into the cells by cells fusion. For this cells entry/cell fusion the spike proteins are crucial. As we have discussed that spikes proteins are structural proteins. Therefore, spikes protein is the potential target for the successful development of anti covid-19 drugs.

Other possible drug's targets are various structural proteins (envelop, membrane, nucleocapsid), haemagglutinin esterase, helicase and protease.

Allopathy has some limitation for the management of viruses and viral disease. Hence, we should have to looks to the alternatives like ayurvedic, homeopathic and other regional medicinal systems. Combination of the knowledge of allopathy and ayurvedic, homeopathy

might be proved to be effective approach for the treatment of novel corona virus/Covid-19.

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Conflict of Interest

None.

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