

COVID-19: ACE-2 Receptor, TMPRSS2, Cathepsin-L/B and CD-147 Receptor

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Keywords

TMPRSS2; ACE-2 Receptor; CD-147 Receptor; COVID-19; Coronavirus Disease; SARS-CoV-2.

Letter to the Editor

COVID-19 shows an extremely rapid spreading pattern, classified as SARS-CoV-2, has become a worldwide health problem. Relating to biological characteristics of SARS-CoV-2, the new viral agent was comprehensively summarized in order to optimize the date research on this novel disease and make adequate therapeutic decisions. The structure of COVID-19 virus is partially similar to SARS-CoV and MERS-CoV and to date, the origin is not clearly ruled out in detail. COVID-19 in general shows, without any adequate measurement, an exponential reproductive rate, an incubation of nearly 14 days. The clinical appearance and the pandemic spread of COVID-19 were very similar to earlier SARS epidemics. The occurrence of SARS-CoV-2; previously provisionally referred to as novel coronavirus 2019 or 2019-nCoV (COVID-19) in China in late 2019, has induced a global spreading and is a worldwide public health problem. At the end of January 2020, the World Health Organization described COVID-19 as the sixth international public health emergency. SARS-CoV-2 is similar to severe corona viruses similar to acute respiratory syndrome of bat origin, bat-SL-CoVZC45 and bat-SL-CoVZXC21. The transmission is based on by human-to-human transmission via droplets or direct contact or stool, whereas the infection seems to have an incubation period of up to 14 days and a reproduction rate of 2.24-3.58. In patients with SARS-CoV-2-induced pneumonia, fever was the prominent symptom in these patients followed by cough. Currently, stopping the rapid spreading of SARS-CoV-2 is the primary intervention in health care management. However, health authorities should continue to monitor the situation closely.

ACE-2 Receptor

The novel coronavirus uses typically angiotensin-II receptor as the way of entry into the pulmonary segments. The SARS-CoV-2 virus docks to the human body with its S-(spike) protein [2,3,6]. The S-

protein shows furin docking site at S1-protein/S2-protein including 12 nucleotides play a role of insertion and moreover and typical, some kind of mutations at the receptor binding domain (RPD) connected with 6 receptor binding domains, amino acids, were ruled out [2,6]. IN relation to the well-known binding site, AT2 blockage could be possible alternative for the disease in childhood [2]. A clinical study with Losartan and Placebo treatment in 200 participants was started in March 2020 in the United States [6]. It is well known to date, expression of ACE2 in pneumocysts type II, in cells of the esophagus, in enterocytes located in the ileum and colon, in cells of cholangial system, in muscle cells of the myocardium and moreover cells of the kidney and the bladder are ruled out. This distribution pattern of ACE-2 and its receptors showed that organs with high ACE2-expressing cells should be classified as potentially at risk for COVID-19 infection. A group of Chinese researchers showed in the study, that ACE2 receptors were highly expressed in the mouth, the tongue, possibly lead to the point that COVID-19 uses an entry to the body in this way [3].

TMPRSS2

The enzymes trypsin, furin and other proprotein convertases, cathepsin, transmembrane proteases (TMPRSS) and elastases play a role in the cell entry of coronaviruses (Coronaviridae) [7,11]. The proteases TMPRSS2 and TMPRSS11a, which are abundant in the respiratory tract and expressed on cell surfaces, promote the entry of the SARS CoV-1 virus. For the TMPRSS protease TMPRSS11d - also known as trypsin-like protease of the human respiratory tract - SARS-CoV has been shown to activate the spike protein proteolytically [8]. TMPRSS2 again reacts in a complex manner with the ACE2 receptor, allowing efficient penetration of the virus directly into the cell surface [8,9,11]. TMPRSS2 and TMPRSS11D activate the spike protein while splitting it into S1 and S2 subunits, allowing endosome-independent cell entry into the cell membrane [8,9].

Cathepsin-L/B

Substantially for the entry the control of spike protein of the virus is by presence of serine protease TMPRSS2 and Cathepsin L. TMPRSS2 activates spike protein for cell-cell and virus-cell fusion in trans-formation only. The S-protein is fusogenetically activated by Cathepsin L, therefore allowing fusion of the viral and endosome membranes. In recent studies, SARS-CoV-2 seems to require a low-pH milieu for infection. Moreover, S protein can induce cell–cell fusion at neutral pH, indicating that S protein-triggered fusion does not include an absolute requirement for an acidic environment. Despite different descriptions, we think that some factors are sensible to NH₄Cl, endosomes that are pH dependent, could influence SARS-CoV-2 entry. The aspects of proteases in viral infectivity and the effects of protease inhibitors on SARS-CoV-2 infection were examined.

Conclusion

SARS-CoV-2 virus needs ACE-2 receptor as host cell receptor to date to our knowledge, the serine protease TMPRSS2 [11], cathepsin L/B (endosome pathway) and, found as an important new docking site, the CD 147 receptor [10]. CD 147 receptor is a type I trans membrane glycoprotein expressed on epithelial cells. A CD147-monoclonal antibody, Meplazumab, was found as add-on therapy in severe cases with cytokine storm immunological situation [10]. Further research in bigger studies with more participants is necessary to closer analyze the exact role of CD 147 receptor and the immunological effect of Meplazumab in COVID-19 pathology [10].

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