ACE2 can be a target for therapeutic purpose of COVID-19

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Letter to editor

It has been demonstrated that the latest outbreak-causing novel coronavirus pneumonia (COVID-19) virus (2019-nCoV, SARS-CoV-2) invades human alveolar epithelial cells primarily by angiotensin-converting enzyme 2 ACE2 (Zhou et al., 2020). The SARS-CoV engages ACE2 for cellular entry to produce final infection (Hoffmann et al., 2020). Furthermore, Zhao et al documented that in human lungs, ACE2 is found primarily in alveolar epithelial cells of type II (AT2), indicating that this virus activates ACE2-positive AT2 cells to cause pneumonia (Zhao et al., 2020). Recently an epidemiological research indicated that certain patients with SARS-CoV-2 exhibit symptoms of severe liver injury (Chen et al., 2020). The investigators also established that ACE2 is significantly enriched in cholangiocytes by studying stable liver cells at single-cell resolution (Chai et al., 2020), depicting that the virus may bind ACE2-positive cholangiocytes directly causes dis-regulation result in liver function. Now the main question arises that why ACE2 is crucial for COVID-19 control and treatment strategies? Normally, ACE2 catalyzing the transformation of angiotensin-II into angiotensin-1–7. Angiotensin-II acts on angiotensin receptor-1(AT1) and controls the processes of vasoconstriction, apoptosis, proinflammatory changes, and fibrosis cycle, while angiotensin 1–7 acts on Mas receptors induces contrary symptoms (Paz Ocaranza et al., 2020). Thus any loss in the activity of ACE2 in the alveolar cells may increase the level of angiotensin II and result in acute respiratory distress. The expression of ACE2 is comparatively higher in lung and a study documented the protective role of ACE2 in lung injury (Imai et al., 2005). It was proved in a mice model that acidic gas inhaled by mice downregulated ACE2 and increased the level of Ang II in the lung and plasma of wild-type mice, and the levels of Ang II in the lung. Further, the research team found that recombinant human ACE2 (rhACE2) protein action may reduce the plasma Ang II levels and reduce the risk of acute lung injury in ACE2 Knockout mice. The binding mode of COVID-19 virus with ACE2 and the clinical importance of renin-angiotensin System, revealed that this system is extensively involved in the pathology of COVID-19 (Gurwitz, 2020; Vaduganathan et al., 2020). Mostly the COVID-19 patients develop fever, inflammatory changes, and respiratory distress. It can be hypothesized that these changes might be due to lack of ACE2 and imbalance in renin-angiotensin system in the pulmonary interstitium. Furthermore, Gurwitz suggested that telmisartan as an alternative choice for treating COVID19 before the respiratory distress develops. Interestingly, Zhang et al. noticed a low fatality rate in COVID-19 hypertensive patients that were exposed to Angiotensin converting enzyme inhibitors (ACEIs) and Angiotensin receptor blockers (ARBs) than control ones (Zhang et al., 2020). Hoffmann and his co-workers proved that protease inhibitor-mediated blocking of Ace2 and Tmprss2 might be a target in the prevention and treatment of COVID-19 (Hoffmann et al., 2020).

Based on the above findings, we can speculate that the treatment strategies for COVID-19 may include recombinant ACE2 therapy, hormones such as estradiol, which increases the level of ACE2, and drugs that decrease the level of angiotensin II.

Keywords: ACE2, Angiotensin II, Zoonosis, COVID19, therapeutic purpose

Ethical approval

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Competing interests

The authors declare that they have no competing interests.

Data Availability

The data is already available in main letter to editor

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