

## COVID-19: The role of Angiotensin-2 Receptor in Transmission Process

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### Short Communication

In early December 2019, a series of pneumonia cases of unknown origin occurred in Wuhan, Hubei Province, China. Most of these patients reported that they had come into contact with many species of live animals in the Huanan seafood wholesale market. In China, the disease has spread rapidly domestically and other parts of the country. It further extended to many countries on 6 continents. On January 3, 2020, a novel member of the enveloped RNA coronavirus was identified in samples of bronchoalveolar lavage fluid from a patient in Wuhan and subsequently confirmed as the cause of the disease by the China Center for Disease Control and Prevention (China CDC). On January 7, 2020, the World Health Organization (WHO) named the virus the new coronavirus 2019 (i.e. 2019-nCoV). On 11 February 2020, the WHO named the disease associated with 2019-nCoV as coronavirus disease 2019 (COVID-19). The appearance of 2019-nCoV has attracted worldwide attention and the WHO has declared COVID-19 a public health emergency of international concern (PHEIC). Worldwide, 693224 cases of COVID-19 infection have been reported since December 2019, including 33106 deaths (WHO, situation report, and date 30-03-2020). In the last 24 hours, 3315 deaths have been recorded worldwide (29-03 to 30-03-2020). These figures show the aggressive and devastating potential of SARS-CoV-2. SARS-CoV-2 binds to angiotensin II receptor at different tissues in the human body, especially in the oral cavity and the tongue. SARS-CoV-2 needs for this binding the serine protease TMPRSS2. SARS-CoV-2 uses the ACE2 receptor as an entry portal into the lungs. The SARS-CoV-2 virus binds to the ACE2 receptor with the spike protein [3]. The spike protein has a functional polyphospho furin cleavage site at S1/S2 by insertion of 12 nucleotides and shows mutations at the receptor binding domain (RBD) with binding to 6 RBD amino acids. In children, more than 80% of angiotensin II receptors belong to subtype AT2, clinically in less severe cases in children. The hypothesis could be that more AT1 receptor bonds of COVID 19 are found in

the more severe case as in adults. This hypothesis needs to be further analyzed by further molecular studies on angiotensin-II receptor binding in severe cases and in children. More than 80% of pulmonary ACE2 is located on type II alveolar epithelial cells that produce pulmonary surfactant [2,3]. Furthermore, a lack of surfactant in newborns leads to ARDS, as in COVID-19 disease. Clinicians should measure surfactant concentrations in children and adults. Due to the binding domain at the angiotensin II receptor, angiotensin receptor blockers are possible alternatives for the treatment of children with severe COVID-19 infection. To date, there is no clinical experience with COVID-19-positive children, nor is there a study on this subject. In adults, a randomized controlled trial (Losartan/Plecebo) for 200 patients with severe COVID-19 infection requiring hospitalization was initiated at the University of Minnesota on March 16, 2020 [5]. The expression and distribution of ACE2 in the human body may indicate the possible routes of infection of 2019-nCoV. Using the developed single cell RNA sequencing technique (scRNA-Seq) and single cell transcriptomes based on the public database, the researchers developed an ACE2 RNA expression profile with single cell resolution. High expression of ACE2 was identified in type II alveolar cells (AT2) of the lung, in upper and stratified epithelial cells of the esophagus, in absorptive enterocytes from ileum and colon, in cholangiocytes, in myocardial cells, in proximal tubule cells of the kidney and in urothelial cells of the bladder. As per results it has been shown that organs with strongly ACE2-expressing cells should be considered potentially at high risk for nCoV infection in 2019 [3]. The study by Xu et al. showed a superiority of COVID-19 virus over ACE2 receptors in the oral cavity and tongue, suggesting that COVID-19 reaches a part of the body by this route [3]. Even more so, it is necessary to wear an oral mask every day in contact with people without clear information about their transmitter status.

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