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Ace 2 Receptor on Oral Mucosa: The Doorway to COVID-19 Pandemic

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ABSTRACT

COVID-19 infectious disease is caused by the most recently discovered coronavirus. This hitherto unknown virus and disease outbreak began in Wuhan, China, in December 2019. COVID-19 pandemic has affected many countries globally. This infection has caused myriad deaths on daily basis. Therapeutic options are currently limited. It has been revealed that COVID19 binds to human angiotensin-converting enzyme 2 (ACE2) to enter the host cells. ACE2, which was discovered in 2000 and is virtually presents in all tissues with relatively higher expression in respiratory epithelial cells, alveolar cells type I and II, oral cavity, kidney, testis, and intestines. Targeting ACE2 receptors may open a new potential therapeutic window for the treatment of COVID-19 before patients enter the irreversible stages.

Keywords- COVID-19, PANDEMIC, ACE2 RECEPTORS,

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INTRODUCTION

The new coronavirus disease 2019 (COVID-19)outbreak has become a global pandemic. The COVID-19 in comparison to the preceding outbreak of brutal Middle East Respiratory Syndrome (MERS-CoV) and Acute Respiratory Syndrome (SARS-CoV) is more contagious and deadly[1]. In March 2020, the World Health Organization (WHO), announced coronavirus as a pandemic and this situation is still deteriorating so far[2]. For the prevention and treatment of COVID-19, we need to explore its pathogenicity and infectious route, despite the fact that, it will be a while before some specific medication and vaccines are developed[3] It has become apparent that, Angiotensin-converting enzyme 2 (ACE2) is the key cell receptor of COVID19 and plays a vital function in the ingression of the virus into the host cell to cause the final infection[4]. As the research of coronavirus goes deepen, this virus was found to be invading in the lung, such as heart, kidney intestines, epithelial cells of buccal mucosa, gingiva, and dorsum of the tongue. Recent reports found that the oral cavity is a functional vector for virus infection, and 2019-nCoV is detected in saliva as well[3,4].

RESEARCH METHODOLOGY

In the present study, an array of sources together with Scopus, Medline, Embase journals, PubMed, and Web of Science has been analysed. This investigation was done by means of the subsequent keywords and or their equivalents; COVID 19, SARS-CoV, oral cavity, saliva, buccal mucosa, ACE2, Coronavirus, and acute respiratory distress syndrome.

INTERACTION BETWEEN ACE2 RECEPTORS AND COVID19 INFECTION

Now, it is well documented that angiotensin-converting enzyme 2 (ACE2) is the chief host cell receptor of human pathogenic coronaviruses(COVID-19), and it plays a vital role in the doorway of the virus into the host cell to cause the final sickness[5]. ACE2 is chiefly expressed via epithelial cells of the lung, kidney, intestine, and blood vessels and this might be the possible explanation of the high prevalence rate of lobar pneumonia and chronic bronchitis in patients suffering from COVID-19 infection[6]. A current study showed that ACE2 is also vastly expressed on the tissues of oral mucosa mainly tongue, gingiva, and buccal mucosa, thus conceding the corona virus easy entrance to a new susceptible host[7]. SARS-CoV-2 binds to angiotensin II receptor at different tissues in the human body, especially in the oral cavity and the cellular protease TMPRSS2 is used for SARS-CoV-2 spike (SARS-CoV-2-S) triggering (Fig. 1)

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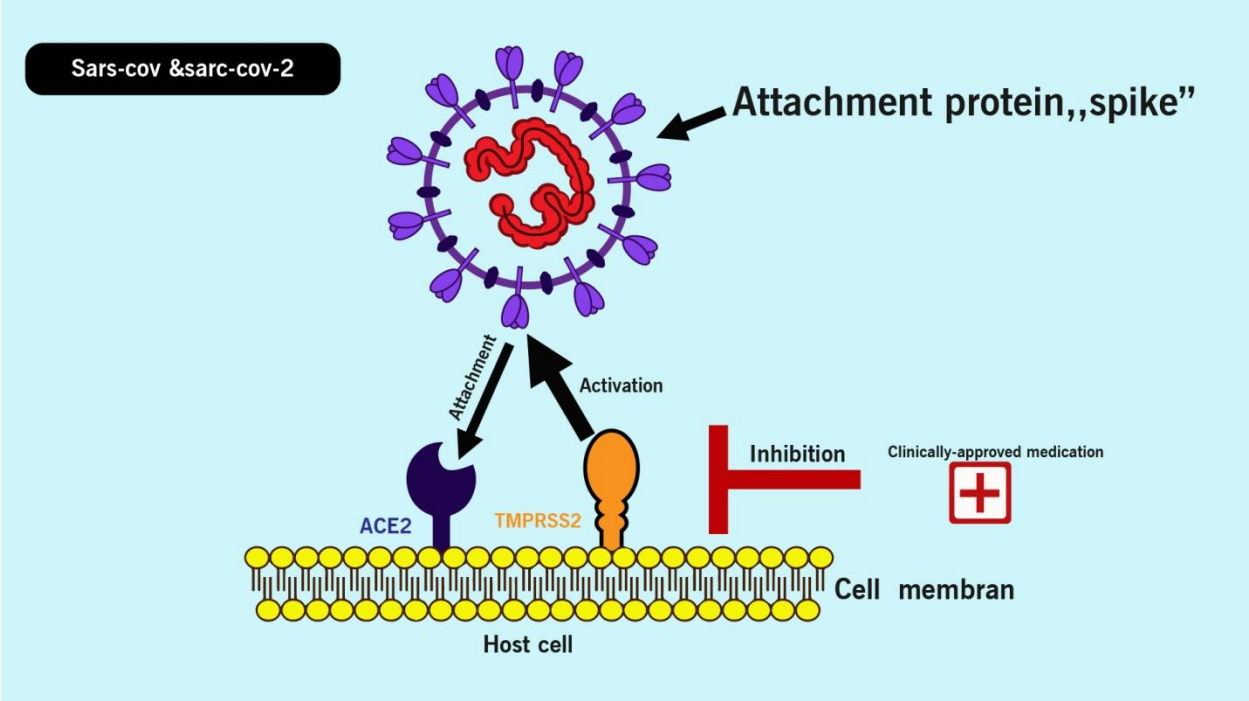

Fig. 1Binding of SARS-CoV-2 to ACE2 Receptor

Both SARS-CoV-2 uses the ACE2 receptor as an entrance portal into the lungs. The SARS-CoV-2 virus binds to the ACE2 receptor through the spike protein[3]. The spike protein has a functional polyphone furin cleavage site at S1/S2 by incorporation of 12 nucleotides and shows mutations at the receptor-binding domain (RPD) with binding to 6 RBD amino acids.

The expression and allocation of ACE2 in the human body may specify a possible route of infectivity of 2019-nCoV. Using the developed single-cell Ribonucleic acid (RNA) sequencing technique (scRNA- Seq) and single-cell transcriptomes as based on the community database, the researchers developed an ACE2 RNA expression outline by means of single-cell resolution. Increased expression of ACE2 was recognized 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 human organs with strongly ACE2-expressing cells should be considered potentially at high menace for 2019-nCoV infection[3]. The study done by Xu et al. showed 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[8].

A POSSIBLE THERAPEUTIC APPROACH FOR COVID-19

On 14th April 2020 Chakraborty et al in his article ACE2 receptor blockers: a novel therapeutic approach for COVID-19 documented that Angiotensin receptor blockers (ARBs) have effects

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that are similar to angiotensin-converting enzyme (ACE) inhibitors. Though, ACE inhibitors act by preventing the formation of angiotensin 2. ARBs are used for regulating hypertension, preventing cardiac arrest and renal failure respectively[4]. Hence, ARBs, for example, telmisartan, losartan, etc could also be a possible new therapeutic approach to prevent the binding of SARS-CoV-2 RBD to ACE2 expressing cells, hence inhibiting its functions[3].Markus Hoffmann et al. in Leibniz Primate Institute, Germany, published an article entitled "The novel coronavirus 2019 (2019-nCoV) uses the SARS-coronavirus receptor ACE2 and the cellular protease TMPRSS2 for entry into target cells" on bioRxiv. It demostrats that SARS- CoV-2 enters the human body through the SARS-CoV receptor ACE2, and the cellular protease TMPRSS2 is used for SARS-CoV-2 spike (SARS-CoV-2-S) triggering. TMPRSS2 inhibitors prevent SARS-CoV-2 entry and are a treatment option[9]. Dr. Robert L. Kruse from Johns Hopkins Hospital in the United States published an article "Therapeutic strategies in an outbreak scenario to treat the novel coronavirus originating in Wuhan, China". It reveals that compared to blockers binding to ACE2 receptors, the use of soluble ACE2 to fuse with the immunoglobulin Fc domain (ACE2-Fc) can block the entry of 2019-nCoV and help the immune system to build lasting immunity. A final benefit of pursuing ACE2-Fc is that it could effectively be used as a therapeutic drug stockpile for future outbreaks of SARS and 2019-nCoV, and any new coronavirus that emerges from a zoonotic reservoir in the future that uses the ACE2 receptor for entry[10]. Chu CM, et al stated that ideal agents to fight 2019-nCoV would be approved small molecule drugs that could inhibit different aspects of the viral life cycle, ultimately inhibiting replication.Two classes of potential targets are viral polymerases and protease inhibitors, both of which are components of human immunodeficiency virus (HIV) and hepatitis C virus (HCV) antiviral regimens.

CONCLUSION

Recent data on the 2019-nCoV and COVID-19 in the oral cavity are valuable and enlightening for a future epidemic prevention strategies. In oral epithelium and salivary glands, the ACE2-expressing cells may provide possible routes of entry for COVID19. And the results that the 2019-nCoV could be detected in oral mucosa not only validate the infectiousness of patient's saliva, also provide a novel ways to monitor the illness state and virus load of patients. Besides the common clinical manifestations, such as fever and cough, we should also pay great attention to the oral symptoms of patients in routine check-ups. The oral examination and interrogation could be meaningful for preventing nosocomial infection and screening the asymptomatic patients of COVID-19 during the current epidemic.

LIMITATIONS

Any other receptors or cellular proteases that involve or might throw more light on the pandemic disease pathogenesis may pave the way to drug therapies. Having a quantitative test of viral load could help direct therapy or detect which patients are likely to decompensate, however, this would take weeks to months of research after the release of a test.

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CONFLICT OF INTEREST

The authors have no conflict of interest relevant to this article.

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