Editorial

Potential Role of Soluble Angiotensin-Converting Enzyme 2 In Salivary Coronavirus Infection Therapy

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Angiotensin-converting enzyme 2 (ACE 2), a monocarboxypeptidase for cleaving several peptides within the renin-angiotensin system and other substrates that are widely expressed in the gastrointestinal tract and the kidneys, with relatively low expression in the lungs [(1)](Figure 1). Interestingly, higher RNA expression of ACE 2 in lung AT2 cells was found in Asian donors, compared to African and white American donors[(2)]. Soluble ACE 2 that lacks the membrane anchor circulates in small volumes in the blood[(3)]. ACE 2 and TMPRSS 2 protein expression are identified mainly in the cytoplasm and cytomembrane of the epithelial cells in the serous acinus cells in submandibular and parotid salivary glands and in vitro, exogenous ACE 2 and TMPRSS 2 can anchor and fuse to human oral mucosa and the spike protein of SARS-CoV-2 can bind to ACE 2 receptors in the salivary glands [(4)]. A recent study demonstrated that during the hospitalization period, 25 % of COVID-19 patients reported of taste impairment, 20 % of patients reported of difficulty in swallowing, and 15 % of patients reported of burning sensation[(5)]. A recent study proposed that chewing gum with SARS-CoV-2-trapping proteins can debulking virus in saliva and minimizing viral transmission[(6)] (Figure 2).

In conclusion, soluble recombinant human ACE 2 protein could be a novel potential biotherapeutic to fight against SARS-CoV-2 and other coronaviruses infection and progression.

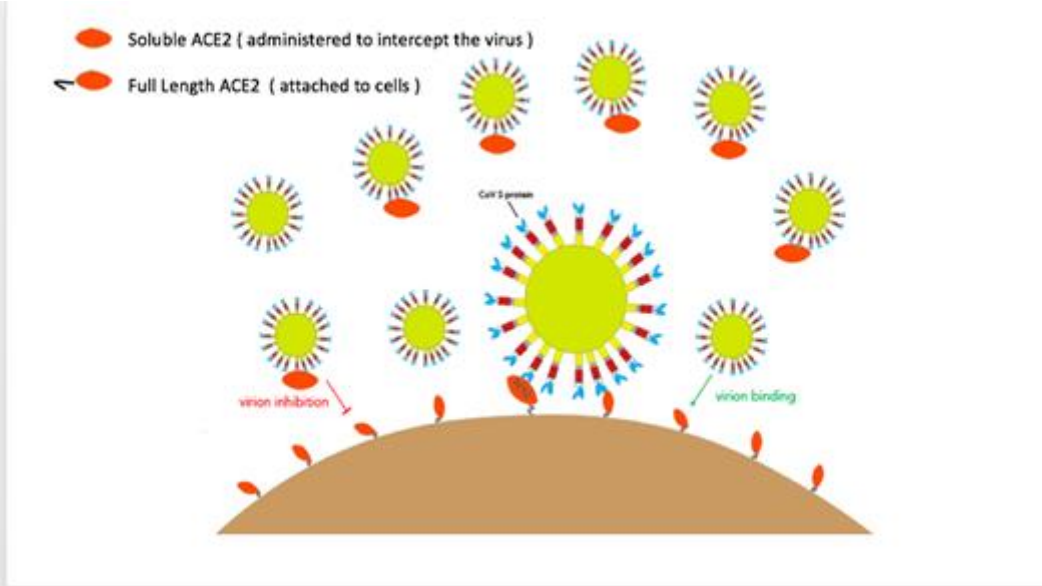

Figure 1 : Demonstrating schematic of coronavirus (CoV) spike protein (S) binding to the surface receptor that is full-length ACE 2 (Soluble ACE 2 administration may prevent binding of the SARS-CoV-2 viral particle to the surface-bound, full-length ACE 2 by acting as a competitive interceptor of SDARS-CoV-2 and other coronaviruses.)
(Source: Battle D, Wysocki J, Satchell K. Soluble angiotensin-converting enzyme 2: a potential approach for coronavirus infection therapy? Clinical Science 2020; 134 : 543-545. DOI: https://doi.org/10.1042/CS20200163)

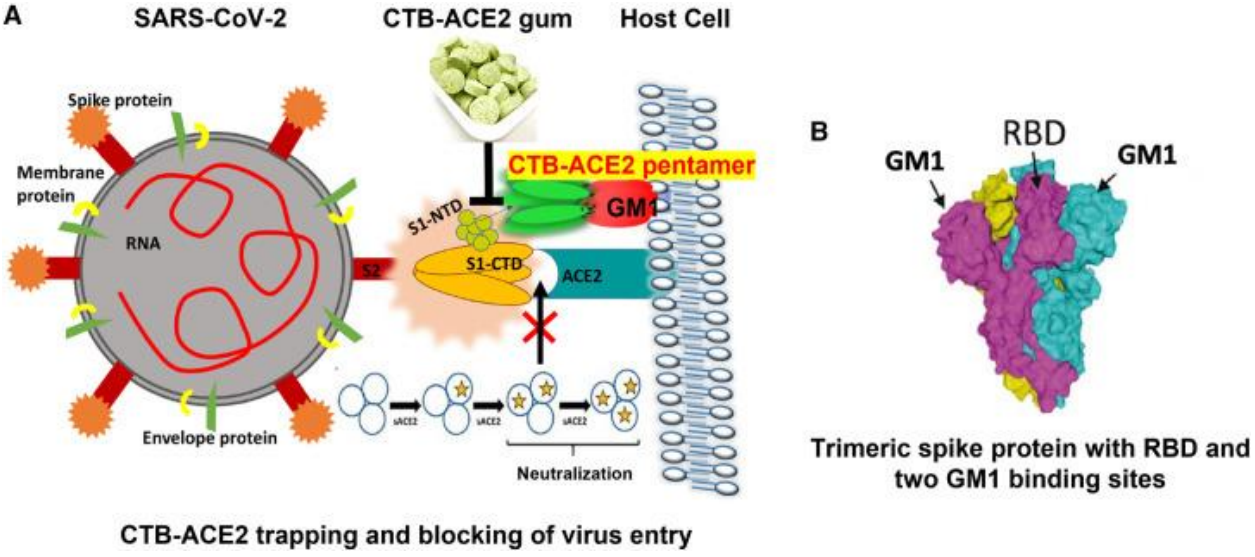

Figure 2 : Demonstrating debulking and blocking of viral entry Using ACE 2 chewing gum

(A): CTB (Cholera Toxin B)-ACE 2 binds to both ACE 2 and GM 1 (monosialotetrahexosylganglioside, prototype of ganglioside) co-receptors

(B): Each SARS-CoV-2 trimeric spike protein has a single RBD (Receptor-Binding Domain) domain and two GM 1 binding sites. CTB-ACE 2 pentamers form microparticles, insoluble and sediment SARS-CoV-2 upon binding to soluble ACE 2, in monomer, dimer, or trimer forms. CTB-ACE 2 also directly binds to ACE 2 and GM 1 receptors, then blocking entry into human or Vero cells.

(Source: Daniell H, Nair SK, Esmaeili N, Wakade G, Shahid N, Ganesan PK, et al. Debulking SARS-CoV-2 in saliva using angiotensin-converting enzyme 2 in chewing gum to decrease oral virus transmission and infection. Molecular Therapy 2022; 30 (4) April 2022. 13 pages. DOI: https://doi.org/10.1016/j.ymthe.2021.11.008)

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