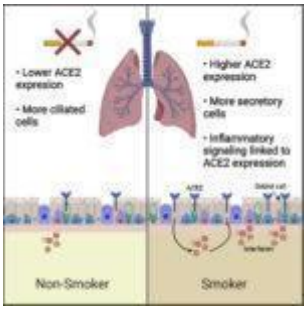
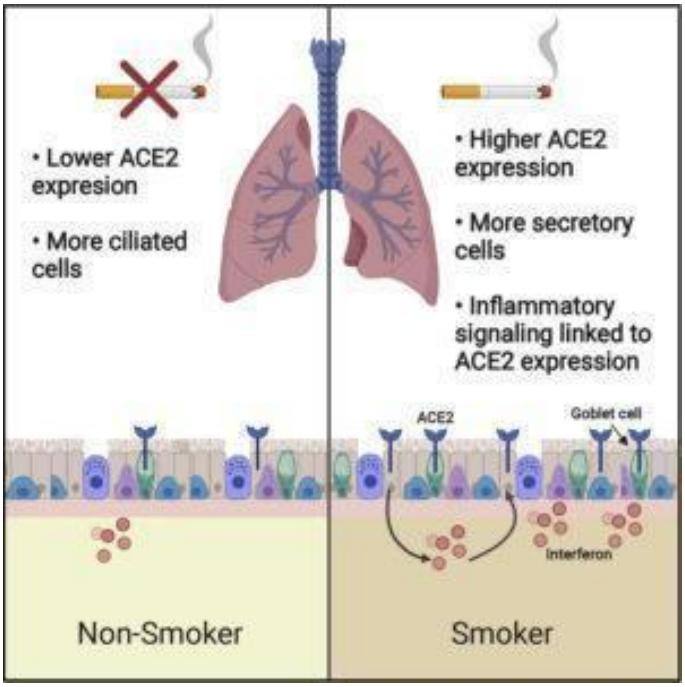
Cigarette smoke triggers increased ACE-2 expression in the lung





Smith et al., 2020. Graphical Abstract

Similar to related coronavirus that emerged in 2003 (1), SARS-CoV-2 enters human cells by binding to the extracellular domain of Angiotensin Converting Enzyme 2 (ACE 2) (2, 3). ACE 2 normally functions in the renin-angiotensin system (RAS) by cleaving the vasoconstrictive hormone angiotensin-II into the vasodilator angiotensin (4). Sequestration of ACE 2 by coronavirus dysregulates the RAS pathway, contributing to morbidity (5). Additionally, modulation of ACE 2 levels is

capable of influencing disease progression, e.g. mice engineered to express human ACE 2 mRNA exhibited short survival time following coronavirus exposure (6). Thus, suggesting that regulation of ACE 2 expression likely has a significant effect on SARS-CoV-2 susceptibility.

Smith, et al., showed that cigarette smoke causes a *dose-dependent upregulation of ACE-2 in rodent and human lungs.* Using single-cell sequencing data, they demonstrated that ACE 2 is expressed in a subset of epithelial cells that line the respiratory tract, including goblet cells, club cells, and alveolar type 2 cells. They showed that cigarette smokers harbor consistently higher levels of ACE-2 in their lungs compared to non-smokers. In contrast, quitting smoking causes a decrease in lung ACE-2 levels. The overabundance of ACE 2 in the lungs of smokers may partially explain why smokers are significantly more likely to develop severe SARS-CoV-2 infections that require aggressive medical interventions (8).

Upregulation of ACE-2 in smokers could be a protective mechanism to prevent lung damage in smokers. However, when a smoker is exposed to SARS-CoV-2 higher ACE-2 expression may facilitate increased viral entry and replication. Taken together, these results may partially explain why smokers are particularly likely to develop severe SARS-CoV-2 infections, and they suggest that quitting smoking could lessen coronavirus susceptibility.

Journal Article: Smith, J. C., et al., (2020). Cigarette smoke exposure and inflammatory signaling increase the expression of the SARS-CoV-2 receptor ACE2 in the respiratory tract. Developmental Cell

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Article by Naffesa Al Sheikh