COVID-19 and nicotine as a mediator of ACE-2

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From the authors:

We recently reported that current smokers and those with COPD had higher airway epithelial cell expression of the angiotensin-converting enzyme II (ACE-2) viral entry receptor [1]. We thus read with great interest the work of P. Russo and co-workers, which proposes a mechanism for this finding, namely that this upregulation is mediated by nicotine exposure specifically through the α7 subtype of nicotine acetylcholine receptors (α7-nAChR). While exposure to increasing concentrations of nicotine caused epithelial cells to increase ACE-2 levels, subsequent gene silencing of α7-nAChR appeared to significantly dampen this response. A secondary transcriptome sequencing analysis of our cohort (consisting of 42 subjects who underwent bronchoscopy for epithelial cell brushings [1]) reveals evidence in support of this hypothesis. We found that airway epithelial cell expression of *CHRNA7*, encoding α7-nAChR, was significantly correlated with the expression of *ACE2* (Pearson r=0.54, $p=2.31\times10^{-8}$) (figure 1). There was significantly higher *CHRNA7* expression in those with COPD (2.75±0.73 *versus* 2.14±0.43 in those without COPD; $p=1.47\times10^{-4}$), with a trend towards higher expression in current smokers compared to former and never smokers (2.86±0.92 in current smokers, 2.35±0.57 in former smokers, and 2.27±0.45 in never smokers; $p=6.16\times10^{-2}$). *CHRNA7* was also negatively correlated with forced expiratory volume in 1 s percent predicted (Pearson r=−0.37, $p=2.83\times10^{-4}$). Interestingly, *CHRNA7* was positively if weakly correlated with body mass index (Pearson r=0.14, $p=6.31\times10^{-3}$), raising the intriguing possibility that nicotine receptor mediation of ACE-2 may also be related to why obese individuals have made up a considerable proportion of coronavirus disease 2019 (COVID-19) cases [2].