The Impact of Smoke Exposure on SARS-Cov-2 Infectivity in Nasal Epithelial Cells

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Abstract

The Coronavirus Disease 2019 (COVID-19) pandemic is an urgent global health crisis that has resulted in over 111,000 deaths to date in the U.S. alone. Although most COVID-19 patients resolve infection with mild/moderate morbidity, some develop severe symptoms, including respiratory failure from acute respiratory distress syndrome (ARDS) driven by abnormally sustained inflammatory cytokine release and alveolar cell damage/death. Cigarette smoking is among the pre-existing conditions associated with worse COVID-19 outcomes, but the link between cigarette smoke exposure and COVID-19 remains poorly understood. COVID- 19 is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which infects cells within the nose that serve as a primary portal for viral entry and act as a reservoir for viral persistence and transmission prior to manifestation of symptoms. Angiotensin-converting enzyme 2 (ACE2), the only experimentally confirmed SARS-CoV-2 receptor, and TMPRSS2, a host cell enzyme that activates viral spike proteins, are key cellular mediators of SARS-CoV-2 infectivity. Recent studies suggest that gene expression levels of ACE2 and TMPRSS2 in nasal and airway epithelial cells may be modulated by cigarette smoking, thereby influencing the ability of SARS-CoV-2 to enter key host cells. In this proposal, we seek to 1) measure the impact of smoke exposure on expression levels of ACE2, TMPRSS2 and viral entry pathway genes in human nasal epithelial cells, 2) determine single cell-level changes in human nasal epithelial cells exposed to cigarette smoke, and 3) characterize single cell-level differences in nasal epithelial cells derived from current versus never smokers. This project will determine whether smoke exposure modulates key SARS-CoV-2 infectivity genes in the human nasal epithelium and identify specific cell types that underlie these differences. Further, this project will determine whether smoke exposure in an in vitro chamber evokes gene expression signatures in nasal epithelial cells similar to those observed in smokers.