

Abstract: The Impact of Tobacco Exposure on the Lung's Innate Defense System  
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Tobacco smoke has a devastating impact on health. Despite evidence that tobacco harms lungs and other organs, >20% of the U.S. population continue to smoke regularly. Tobacco smoke causes COPD and lung cancer. Long term tobacco exposure triggers an inflammatory response in the lung that contributes to the pathogenesis of COPD. Moreover, COPD is a common and important independent risk factor for lung cancer and thus, COPD may be thought of as a pre-cancerous state. More specifically, tobacco smoke causes airway surface liquid/mucus dehydration and increased incidence of viral infections, suggesting that the Lung's Innate Defense System has been impaired. These changes are thought to contribute to the pathogenesis of COPD. In response to new legislation aimed at curbing the sale of cigarettes, the tobacco industry has developed tobacco alternatives that seek to evade this legislation. Usage of "little cigars" which are often flavored and are thus attractive to younger smokers has risen 240%. While in NC, up to 50% of college students claim to have tried Hookah, with >10% being regular Hookah smokers. Whilst many of these tobacco alternatives are perceived to be "safer", their impact on lung health is unknown. Thus, we propose to measure the potential adverse impact of tobacco alternatives on the lung's innate defense system. Projects I and II (Tarran and Kesimer) are focused on determining the impact of tobacco alternatives on specific aspects of this system, namely, airway surface liquid homeostasis and mucin/mucus and will use an innovative in vitro smoke exposure system to measure specific biomarkers of innate lung defense as well as obtain airway samples from smokers of alternate tobacco. In Project III (Doerschuk), we propose to develop a novel animal model of smoke exposure that more closely mimics the chronic bronchitis phenotype seen in humans with COPD. This model will be used to validate tobacco exposure biomarkers seen in Projects I and II as well as to determine epigenetic changes following in vivo exposure to alternative tobacco. Project IV (Jaspers) will determine genomic biomarkers associated with tobacco alternatives from samples obtained from human volunteers. Focusing on changes in antiviral host defense in these subjects, this model will be used to integrate observations made in the other projects with findings obtained from humans infected with live attenuated influenza virus. Thus, using human and mouse in vivo and in vitro models, this project will identify novel biomarkers associated with tobacco-induced changes in lung innate defense, which can be applied to understand potential toxicity of any new and emerging tobacco products.