Abstract: Overlapping airway basal cell transcriptome reprogramming in COPD and lung cancer
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In response to PAR-12-010 based on the Family Smoking and Tobacco Control Act, this proposal is a logical expansion of our current grant R01 HL107882 "Overlapping Airway Basal Cell Transcriptome Reprogramming in COPD and Lung Cancer." Specifically, it is in response to the PAR-12-010 priorities of the "the toxicity and use of new and emerging tobacco products." Our focus is on the effect of shisha smoking and electronic cigarette smoking on the biology of the small airway epithelium, the initial site of lung pathology associated with cigarette smoking. In the current grant, we recover small airway epithelium from cigarette smokers, smokers with chronic obstructive pulmonary disease (COPD), and smokers with lung cancer with and without COPD, and compare the disordered biology of the recovered cells to that of healthy nonsmokers. In this new proposal, **we hypothesize that shisha smoking or electronic cigarettes disorder airway biology, but this disordered biology differs from that resulting from cigarette smoking, suggesting that these alternative nicotine delivery methods will cause lung disease, but perhaps with phenotypes different from that of cigarette smoking.** This is a rational expansion of the parent grant since both involve molecular analyses of the impact of nicotine delivery systems (parent grant – cigarettes; current grant – shisha and electronic cigarettes) on the airway epithelium. The parent application has additional aims related to the basal cell stem / progenitors that give rise to the whole epithelium, while this application focuses on the intact epithelium that arises from basal cell differentiation. Since essentially nothing is known about the effect of shisha or electronic cigarette smoking on the airway epithelium, whereas the parent grant focuses on the basal cell population of the airway epithelium, in the proposed grant to assess shisha and electronic cigarettes, we will take a step back and assess the effect of these alternative nicotine delivery systems on the biology of the entire population of small airway epithelial cells. The biological materials collected (airway epithelium from well-phenotyped subjects) and analytical methods focused on gene expression profiling are similar. The rationale is to understand the extent, if any, to which these alternative nicotine delivery systems disorder airway biology, and whether these changes are similar or different from that of cigarette smokers. Based on our extensive data on the changes in airway biology associated with cigarette smoking, and preliminary data with shisha smoking, the proposed studies will provide a comprehensive molecular catalog of the changes in the airway epithelium associated with shisha and electronic cigarette smoking, providing insight that will guide relevant public health education and regulatory measures related to what are advertised as "safe" nicotine delivery approaches.