**Project Title: The Impact of Vape Use on Nasal Epithelial Gene Expression in Latino Youth**

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**Background and Significance:** Recent estimates of vape use initiation among youth in the United States have been called an epidemic(1) with an increase of 10% among 12th graders in 1 year(2). Increased use of vaping has been identified specifically among Hispanic/Latino youth at alarming rates much higher than non-Hispanic youth(3). Colorado is a leader in electronic smoking device use among teenagers. In Colorado 48.3% of Latino high school youth reported ever having vaped and recent national reports showing disproportionately higher electronic smoking device use among Latino youth. Short-term exposure to e-cigarettes in healthy adults increases airway resistance, with some evidence demonstrating decreased lung function after exposure(4). However, the biologic determinants of reduced lung function have yet to be elucidated. Since previous investigations have demonstrated that nasal epithelial gene expression is a non-invasive measure highly correlated with gene expression in the bronchial epithelium(5), we propose to compare nasal epithelial gene expression in adolescent subjects who vape to non-vaping controls to determine the biological impact of vape exposure.

**Study Population:** We are currently collaborating with the Pueblo Department of Public Health and Environment (PDPHE) in a mixed methods study to assess the reasons for vaping initiation and the respiratory effects of vape use in Latino youth (middle and high school age). After assent has been obtained from each child, Latino adolescents participate in focus groups on reasons for vaping initiation, a confidential survey on their own vaping use, measurement of lung function, and a nasal epithelial brush sample collection. Although funding has been obtained from the Latino Research and Policy Center for the focus groups and lung function measurement, additional financial support for nasal epithelial gene expression profiling has not been secured. For this pilot study, we propose the following specific aims:

**Aim 1: The Gene Expression Signature of Vape Use in Latino Youth: We hypothesize that nasal epithelial gene expression is modified by vape exposure.** We will characterize the nasal epithelial gene expression signature of vape exposure in Latino youth by performing RNA-sequencing (RNA-seq) on 5 vape-exposed youth and 5 non-vaping control subjects. We will identify the genes that are differentially expressed between vape exposed and non-exposed individuals using linear models adjusted for age, comorbidities, and medication use.

**Aim 2: Nasal Epithelial Gene Expression Changes Related to Vape Exposure are Associated with Lower Lung Function in Latino Youth: We hypothesize that gene expression changes due to vape exposure identified in the nasal epithelium of Latino youth are associated with increased airway resistance.** We will also test the genes identified in Aim 1 for association with measures of abnormal lung function using linear models with appropriate covariate adjustment.

**Approach:** We will perform nasal epithelial gene expression profiling on 5 vape-exposed and 5 non-exposed Latino youth collected on subjects participating in our Latino Youth Vaping Project (see above). Nasal epithelial brush samples for RNA-seq have already been collected. RNA will be extracted using the Qiagen RNeasy Mini Kit (Qiagen, Valencia, CA) and sequenced using the Illumina HiSeq platform through the Genomics Core. We will use a generalized linear mixed model (GLMM; random patient intercept) to model levels of nasal epithelial gene expression by exposure status, controlling for possible confounders such as age, sex, medication regimen. Finally, we will use Ingenuity Pathway Analysis in exploratory analyses to examine the differentially expressed genes for enrichment of known biological pathways. We will also use moderated t-tests as implemented in the Limma software package to assess gene expression association with measures of lung function with appropriate covariate adjustment. The overarching goal of this proposal is to identify the gene expression changes due to vape exposure in Latino Youth and to determine if these changes are associated with abnormal lung function. In addition, this project will provide critical preliminary data for a future R01 investigating the impact of vape exposure on nasal epithelial gene expression and abnormal lung function in vaping youth and how these changes are impacted by an intervention cessation program that we hope to put in to the National Heart Lung and Blood Institute in Feburary.

**References:**

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