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 show disproportionately higher electronic smoking device use among Latino youth. Thus, the prevention of youth initiation of both electronic and combustible smoking is required. While national surveys have identified the increased initiation of electronic smoking device use among Latino youth, they have not been able to assign causes for the disproportionate use. Furthermore, evidence-based treatment programs for nicotine dependence among youth are lacking while prevention programs for electronic smoking device initiation are in their infancy. To date, very little is known about the behavioral aspects of vape initiation and barriers to quitting amongst the Latino adolescent population. Furthermore, the health implications of vape use on the respiratory system in young adolescents is not yet known. 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 to investigate the impact of vape exposure on airway biology.

**Aim 1: Develop a comprehensive description of Latino youth electronic smoking device behaviors to inform preventive and control strategies.**

**Sub-Aim1:** Describe the electronic smoking device use and access among Latino youth across Colorado.

**Sub-Aim 2**: Pilot intervention

**Aim 2: The Impact of Vape use on Respiratory Outcomes**. We hypothesize that vape use is associated with increased airflow obstruction and airway inflammation in Latino youth. We will investigate the impact of vape use on respiratory outcomes by testing for its association with spirometric measures of lung function, impulse oscillometry, and exhaled nitric oxide by comparing adolescents who vape versus non-vaping controls.

**Aim 3: The Gene Expression Signature of Vape Use in Latino Youth: We hypothesize that nasal epithelial gene expression is modified by vape exposure and is associated with increased airway resistance and airway inflammation.**

**Sub-Aim 1:** We will characterize the nasal epithelial gene expression signature of vape exposure in Latino youth by performing RNA-sequencing (RNA-seq) on 50 vape-exposed youth and 50 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.

**SubAim 2:** We will also test the genes identified in Aim 3 Sub-Aim 1 for association with measures of abnormal lung function, impulse oscillometry, and exhaled nitric oxide using linear models with appropriate covariate adjustment and assess for enrichment of genes in inflammatory pathways using gene set enrichment analysis.

The overarching goal of this project is to develop a comprehensive description of Latino youths’ electronic smoking device behaviors and to investigate the impact of vape use on the airway epithelium and respiratory outcomes. In addition, this project will provide critical preliminary data to design of electronic smoking prevention, treatment, and control programs specifically tailored for Latino youth.

**References:**

1. Radio NP. Surgeon General Warns Youth Vaping Is Now An 'Epidemic'. Aired on December 18, 2018. <https://www.npr.org/sections/health-shots/2018/12/18/677755266/surgeon-general-warns-youth-vaping-is-now-an-epidemic>; December 18, 2018.

2. Miech R, Johnston L, O'Malley PM, Bachman JG, Patrick ME. Adolescent Vaping and Nicotine Use in 2017-2018 - U.S. National Estimates. *N Engl J Med* 2019; 380: 192-193.

3. Hammig B, Daniel-Dobbs P, Blunt-Vinti H. Electronic cigarette initiation among minority youth in the United States. *Am J Drug Alcohol Abuse* 2017; 43: 306-310.

4. Chun LF, Moazed F, Calfee CS, Matthay MA, Gotts JE. Pulmonary toxicity of e-cigarettes. *Am J Physiol Lung Cell Mol Physiol* 2017; 313: L193-L206.

5. Boudewijn IM, Faiz A, Steiling K, van der Wiel E, Telenga ED, Hoonhorst SJM, Ten Hacken NHT, Brandsma CA, Kerstjens HAM, Timens W, Heijink IH, Jonker MR, de Bruin HG, Sebastiaan Vroegop J, Pasma HR, Boersma WG, Wielders P, van den Elshout F, Mansour K, Spira A, Lenburg ME, Guryev V, Postma DS, van den Berge M. Nasal gene expression differentiates COPD from controls and overlaps bronchial gene expression. *Respir Res* 2017; 18: 213.

We evaluated the statistical power to detect differences in average gene expression between vape exposed and non-exposed groups using the ssizeRNA software package (citation). We assumed mean and variability in genes similar to preexisting nasal epithelium RNA-sequencing data obtained from a similar population (non-asthmatic Latino adolescents, citation) obtained using a similar experimental and computational protocol as proposed here. Assuming 16,000 genes tested (pre-filtering of lowly expressed genes in reference dataset, average counts per million < 0.5) and assuming that only 10% of genes are truly differentially expressed, at a statistical significance threshold of FDR < 0.05 and N = 50 participants per exposure group, we can detect low-to-moderate effect sizes (fold-change = 1.5) with an average of 91% power.