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**Scientific Abstract**

Specific aims:

1. Characterize the association between tobacco and oral health in 11,000 subjects in the 2009-2012 NHANES study, a nationally representative sample of the U.S. population with oversampling of persons 60 and older, African Americans, Asian-Americans, and Hispanics and extensive exposure and health information.
2. Investigate the association between types of tobacco use and the oral microbiome
3. Investigate the association between the oral microbiome and tobacco-related diseases including periodontitis, cardiovascular and respiratory disease, diabetes, and others in NHANES and investigate the degree to which the oral microbiome mediates the adverse health effects of tobacco use

Tobacco use is a strong risk factor for poor oral health. Although tobacco use and poor oral health have been associated with a wide range of diseases including cancer, cardiovascular disease, and diabetes, the effect of tobacco use on the bacteria in the mouth, the oral microbiome, has been poorly studied. We propose to address these questions in two National Health and Nutrition Examination Survey (NHANES) study cycles. The proposed study will be the first to comprehensively characterize the effects of tobacco on the oral microbiome, and is strengthened by using a representative sample of the U.S. population. Identifying the effect of smoking cigarettes and chewing tobacco on the oral microbiome will also produce new biomarkers of exposure that can be used to assess the effects of new and emerging tobacco products. As part of an ongoing oral HPV study in NHANES, oral rinse samples are being collected from approximately 11,000 men and women aged 14-69 years. Approximately 55% of participants will be never smokers, 20% will be former smokers, 23% will be current smokers, and 2% will be tobacco chewers. In addition to the comprehensive examinations typically part of NHANES, half the subjects in the proposed study (the 2011-2012 cycle) also include especially detailed oral health assessment with a full mouth periodontal and caries exam. The oral microbiome will be measured in DNA extracted from oral samples by high-throughput sequencing of the bacterial 16S rRNA gene. We will quantitatively describe the bacterial species in each sample. We will use bacterial identity and  $\alpha$ - and  $\beta$ -diversity metrics to examine the effect of tobacco on the full microbiomic community, determine whether associations vary by type of tobacco used (e.g. cigarette brand, menthol, filter, smokeless), household tobacco exposure, or ethnicity, and evaluate associations with tobacco-related diseases.