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Scientific Abstract

This project is a collaborative investigation into the role of inherited differences in taste perception in tobacco use, taking advantage of our substantial experience in the genetics of human taste perception and the role of taste variation in tobacco use. We will catalog and quantify the variation in genes that encode the taste perception system and use these to measure association between taste-specific genetic variants and tobacco use in a large multi-ethnic U.S. population sample. This will include studies of the genes encoding receptors for menthol (TRPM8), bitter (TAS2R gene family), sweet and savory (TAS1R gene family), sour (PKDL gene family), and burning (TRPV1 gene) tastes. It also includes genes encoding the downstream signaling components in taste cells, including the GNAT3, GNB3, GNG13, and PLCB2 genes. These variants will be assayed in the Dallas Heart Study (DHS) population, a group of 4,700 subjects, including 2,500 African Americans, that has been well characterized for cardiovascular risk factors including tobacco use. Existing genotypes typed at 20,000 loci across the genome in the DHS population will be evaluated directly to generate measures of linkage disequilibrium and haplotypes that can impute genotypes at taste perception gene loci, as well as at coding and non-coding loci across the genome. This medium-resolution data will allow association studies with tobacco use phenotypes to begin immediately, and can identify associations with tobacco usage that reside outside known taste perception gene loci.

To gain additional power in this sample, we will make a more global analysis of genetic differences in the subset of DHS subjects who display extreme phenotypes. This will consist of whole-exome sequencing in a total of 1700 subjects, half representing the lowest 12.5 percentile and half representing the highest 12.5 percentile of the distribution of scores on measures of daily tobacco use frequency and use of mentholated cigarettes. Whole exome sequencing is expected to enumerate all of the sequence variants that exist in the expressed portion of the genome, including known taste perception genes and perhaps other genes not yet known to be involved in taste perception.

Correlations between genetic variants and tobacco use behaviors, including the use of mentholated tobacco products, will be determined. These analyses will involve genotype-phenotype association tests using linear regression, as well as a novel approach for testing associations in aggregate. The overall goal of this project will be to disentangle the relative roles of genetic sensory factors present in specific populations, including African Americans, from environmental and other non-genetic factors in tobacco use.