The use and abuse of alcohol and nicotine has a significant impact on public health. Twin and family studies show that these behaviors have a significant genetic component. Genetic association studies have discovered common variants associated with alcohol and nicotine. The exome chip portion of the GWAS & Sequencing Consortium of Alcohol and Nicotine Use (GSCAN) was formed to examine the association between rare nonsynonymous variants and alcohol and nicotine use, by aggregating and meta-analyzing studies using exome sequencing or genotyping arrays with substantial rare exonic content. We performed extensive quality control and phenotype standardization, followed by rare variant association analyses for five phenotypes: smoking initiation (total N=164,142), cigarettes per day (total N=75,493), age of initiation of smoking (total N=64,616), pack years (total N=72,909), and drinks per week (total N=139,103). We find significant novel associations between cigarettes per day and a variant in \textit{STARD3} and two intergenic variants on chromosome 19. The variant in \textit{STARD3} failed to replicate in two independent datasets: the CHD Exome+ Consortium (N=17,789, p=0.94) and the Consortium for Genetics of Smoking Behaviour (N=28,583, p=0.84). Replication is pending for the intergenic variants. We also replicated the classic association of \textit{ADH1C} with alcohol use in both single variant and gene based tests. The GSCAN project is also performing a GWAS analysis of alcohol and tobacco use phenotypes, with sample sizes
currently as high as 238,045 individuals for smoking initiation. We are currently meta-analyzing these results and expect additional studies to contribute.