

Submitter Name: Chelsie Benca-Bachman
Submitted email: chelsie.benca@emory.edu
PI Name: Rohan Palmer
PI email: Rohan.Palmer@Emory.edu

Cross-Species Prioritization of Genomic Loci for Nicotine Consumption

Chelsie Benca-Bachman¹, Jason Bubier², Nikhil Ramgiri¹, Jenani Srijevanthan¹, Elissa Chesler²,
Rohan Palmer¹,

¹ Department of Psychology, Emory University; ² The Jackson Laboratory

Computational advances have fostered development of new methods/tools to integrate gene expression and functional evidence into human-based association analyses. Integrative functional genomics analysis for altered response to alcohol in mice provided the first evidence that resources, such as GeneWeaver, can identify/confirm novel alcohol-related loci. The present study investigates how highly-connected genes linked by their association to tobacco-related behaviors, contribute to individual differences in nicotine consumption. Data from individuals of European ancestry in the UKBiobank (N=139,043) were used to examine the relative contribution of sets of genes that are transcriptionally co-regulated by tobacco/nicotine exposure. Gene sets were limited to those from curated studies focused on differential expression in model organisms; human candidate gene and GWAS studies were excluded. Intersection among the gene sets was determined using the maximal biclique enumeration algorithm implemented in GeneWeaver's Hierarchical Similarity Graph function. Approximately 900 genes were identified across studies of nicotine consumption across model organisms (mice, rats, *c. elegans*, and *drosophila*) via GeneWeaver for nicotine; no weighted gene co-expression network analysis (WGCNA) studies using paradigms for withdrawal or craving were identified. We discuss the relevance of genetic variation across loci within and around (i.e., within 5/10 kb of each gene) each gene set to the heritability of nicotine consumption in humans. Models were fitted using mixed linear model association analyses and genome-based restricted maximum likelihood. These results describe how well highly represented genes among our gene sets can be incorporated in genomic prediction studies of nicotine/tobacco use behaviors.