NIDA Genetics Consortium Genome-wide Association Study of Opioid Addiction – Wave 1

*NIDA Genetics Consortium GWAS of OA Investigators**

Prevalence of addiction to the opioid drug class is growing dramatically, as are the public health consequences (e.g., increasing overdose deaths for 14 consecutive years). Heritability of opioid addiction is substantial (~60%). However, after more than 30 years of research, including six genome-wide association studies (GWAS) and numerous linkage and candidate gene studies, independently replicable associations have been found only recently for variants in the opioid receptor genes *OPRM1* and *OPRD1*. Three recent GWAS (largest discovery N=5,697) have reported genome-wide significant loci, but all await independent replication. In contrast, recent GWAS by the Psychiatric Genetics Consortium (PGC) for schizophrenia (N = 150,064), and other psychiatric phenotypes, have been highly successful (108 loci for schizophrenia), illustrating the critical need for large sample sizes in complex disease GWAS. Against this backdrop, NIDA Genetics Consortium (NGC) GWAS of Opioid Addiction (OA) was born during the June 2017 NGC meeting. Here we will report on the Wave 1 collaborative meta-analysis of 19 cohorts across three phenotypes: OA vs. all controls (case N=13,555; control N=48,238); OA vs. exposed controls (case N=4,388; control N=3,779); and frequency of opioid use among users (user N=14,403). The NGC OA GWAS uses a broad definition of cases and controls, using multiple methods to define cases (e.g., frequency of use thresholds, qualifying for methadone maintenance treatment, DSM diagnosis) and controls (e.g., assessed controls and unassessed population controls). This effort parallels the PGC –Substance Use Disorder (SUD) GWAS of opioid dependence, which focuses on cases defined by DSM diagnostic criteria and assessed controls. Overlapping and differential gene variant discoveries from the NGC and PGC-SUD efforts will be highly informative for gene discovery and future study design. We further anticipate doubling our sample size for Wave 2, which will incorporate new cohorts being genotyped under individual projects or through the NIDA Smoke Screen initiative.

* corporate authorship representing all contributing cohorts and investigator affiliations. Submitted by Eric O. Johnson on behalf of the consortium.