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CONSILIENCE-GWAS: A Web Resource for Parsed Heritability & Polygenic Score Analysis of Human GWAS Using Heterogeneous Functional Genomics Data

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Background: Addiction-related genomewide association studies (GWAS) are important in understanding risk for substance use and disorders. However, there are no resources that allow for a comprehensive assessment and integration of functional knowledge from model system experiments. We address this technological gap by introducing the CONSILIENCE webtool that simplifies the aggregation, analysis, and visualization of the enrichment of functional data in GWAS.

Rationale/Significance: GWASs have begun to identify loci associated with substance use and disorders, but most associated loci reside in intergenic regions necessitating functional evidence to translate and prioritize loci for further study. Data depots of functional evidence in tissues, cell types, and experimental paradigms across organisms hold significant promise when integrated with GWAS results. Yet, enrichment analyses accounting for these effects across species are limited despite the existence of information resources that house diverse model organism data.

Results: CONSILIENCE investigates how GWAS data are enriched by model system evidence. CONSILIENCE incorporates enrichment pipelines and parameters for LD Score Regression and gene-set based polygenic score creation of user-supplied GWAS summary statistics and genotype data. CONSILIENCE integrates with GENEWEAVER via APIs, allowing end-users to upload, curate, compare, analyze, and share their results. We demonstrate features of CONSILIENCE via novel use cases for enrichment analysis of alcohol consumption phenotypes in *Mus musculus* translated to human GWAS of alcohol use and disorder.

Discussion: CONSILIENCE is supported by DP1DA042103 and is freely available at https://consilience.bgalab.emory.edu/enrichment_V2.html. This open sourced tool will help accelerate future translational genomic studies and the interpretation of complex biological data.