

Heterogeneous functional genomics data integration for addiction biology

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Discovery of molecular and neurobiological mechanisms of addiction and addiction vulnerability can lead to insights into prevention and therapeutic interventions. Functional genomics technologies provide a wealth of data for identification of mechanisms for various endpoints, and the use of animal experimentation enables exquisite investigation of precise aspects of behavioral processes. However, questions about construct validity of animal phenotypes to addiction related behaviors in humans remain, as do questions about the convergence of biological substrates across species. Advances in heterogeneous data integration enable the simultaneous classification and identification of addiction related behaviors within and across species. Two approaches to data integration, systems or integrative genetics and integrative functional genomics enable the comparison of results across laboratories, paradigms, populations and species to relate endpoints and their molecular substrates. Systems or integrative genetics relies on genetic reference populations to correlate genetic, molecular, neurobiological and behavioral measures curated in the Mouse Phenome Database to discover and identify the biological basis for relations among multi-scalar traits. By exploiting genetic meta-analysis and ontology annotations, more generalized data integration is enabled. This approach is deployed within populations and can feed, along with other functional genomics approaches, the aggregate analysis or molecular mechanisms across traits. Integrative functional genomics uses combinatorial methods to compare, contrast and classify behavioral endpoints within and across species through common and distinct molecular mechanisms. This approach, deployed in GeneWeaver.org enables the identification of the shared processes underlying the biological concepts reflected in functional genomic experimental results and curated data resources, including genes associated with behavioral traits. Through these tools and approaches, diverse biobehavioral processes and stages of addiction can be related to one another and harnessed to identify mechanisms and interventions for substance use disorders.

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