THE HYBRID RAT DIVERSITY PANEL FOR ADDICTION RESEARCH

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One of the most important resources for systems genetic studies is a genetically stable (isogenic) panel of strains, which allows for fine mapping of complex phenotypes (QTLs) and provides statistical power to identify loci which contribute nominally to the phenotype. Often, rats are preferred over mice for physiologic and behavioral studies because of their larger size and more distinguishable anatomy (particularly for their CNS). The Hybrid Rat Diversity Panel (HRDP) is such a panel of rat strains, which combines two recombinant inbred panels (the HXB/BXH, 30 strains; the LEXF/FXLE, 33 strains and 33 more strains of inbred rats which were selected for genetic diversity, based on their fully sequenced genomes and/or thorough genotyping). The HRDP will provide a genetically stable group of animals whose genomes are well-sequenced (30x) and the total RNA (coding, non-coding, large, small) of brain, liver and heart will be characterized by RNAseq. The RNA will be mapped to the genome, annotated as possible, and assigned to modules and networks by use of WGCNA. The QTLs for individual transcripts and module QTLs will also be available for integration with phenotypic QTLs. The HRDP will be particularly suited to investigations of predisposition or susceptibility loci for physiologic and pathologic phenotypes. Although the completion of the HRDP is a work in progress, sufficient work has been performed and analyzed to provide confidence that this resource will well serve the addiction research community. The genomic sequence of the progenitors of the HXB/BXH panel has been completed and is available, as is the imputed sequence of the 30 RI strains of this panel. The genomic sequence of an additional 10 inbred strains of HRDP is also available. RNAseq data for brain, left ventricle of heart, and liver are also available as are data on cell-specific RNA expression in liver (hepatocyte, Kupffer, stellate and endothelial cells). All data have been quality controlled, normalized and cleaned and are available in this form, or as raw data. The data are also available in visualization formats using genome tracks and network/QTL visualization tools. The portal to access all information and tools is http://phenogen.ucdenver.edu. A number of publications have been generated using the data on just the HXB/BXH RI strains and this work has identified a viable pipeline for incorporating genomic, transcriptomic, and phenotypic data into a systems analysis of biologic diversity leading to individual differences in predisposition to behavioral and physiologic phenotypes (supported by R24 AA013162 and the Banbury Fund).