

Submitter Name: Oksana Polesskaya  
Submitted email: [opolesskaya@ucsd.edu](mailto:opolesskaya@ucsd.edu)  
PI Name (if different): Oksana Polesskaya  
PI email (if different): [aapalmer@ucsd.edu](mailto:aapalmer@ucsd.edu)

### **High-throughput genotyping of HS rats using low-coverage sequencing.**

Oksana Polesskaya<sup>1</sup>, Riyan Cheng<sup>1</sup>, Apurva S Chitre<sup>1</sup>, Denghui Chen<sup>1</sup>, Bonnie Lin<sup>1</sup>, Abraham Palmer<sup>1,2</sup>

<sup>1</sup>Department of Psychiatry, University of California San Diego; <sup>2</sup>Institute for Genomic Medicine, University of California San Diego

Heterogeneous stock (HS) rats are the most widely used outbred rat population because they provide the best mapping resolution and genetic diversity. HS rats were derived from eight inbred strains and maintained over 90 generations ago, and have been maintained as a large outbred colony since their inception. The NIDA Center for GWAS in Outbred Rats is using HS rats to study genetic underpinning of complex behavioral traits related to drug addiction. In the next 4 years, we expect to genotype at least 8,000 HS rats. We have developed a cost-effective and high-throughput genotyping method that is based on low-coverage sequencing. Libraries are prepared using Riptide (iGenomX), which is a low cost whole-genome library preparation kit, and then sequenced (Illumina NovaSeq 6000) to obtain  $\geq 0.2x$  coverage. Our bioinformatics analysis takes advantage of the fact that HS founders have been fully sequenced: the founders' genomes are used as a reference panel for STITCH. We use BWA for mapping, STITCH for variant calling and then BEAGLE for imputation to reference. We are able to call more than 8 million SNPs with 99% accuracy. As the number of animals that we have sequenced grows, so does our ability to call novel SNPs and other features, including those that may not have been present among the founders. We are also using this genotyping pipeline for other populations and species; for example, we have successfully genotyped Sprague-Dawley rats, *Peromyscus californicus* and zebrafish.