Structural variants in heterogeneous stock rats

<u>Denghui Chen¹</u>, Khai-Minh H Nguyen², Milad Mortazavi², Daniel Munro^{2,3}, James Guevara², Katarina Cohen², Melissa Gymrek^{4, 5}, Jonathan L Sebat^{2, 6, 7}, Abraham A Palmer^{2, 6}

- ¹ Bioinformatics and System Biology Program, University of California San Diego, La Jolla, CA, USA
- ² Department of Psychiatry, University of California San Diego, La Jolla, CA, USA
- ³ Center for Immunity and Immunotherapies, Seattle Children's Research Institute, Seattle, WA, USA
- ⁴ Department of Computer Science and Engineering, University of California San Diego, La Jolla, CA, USA
- ⁵ Department of Medicine, University of California San Diego, La Jolla, CA, USA
- ⁶ Institute for Genomic Medicine, University of California San Diego, La Jolla, CA, USA
- ⁷ Department of Cellular and Molecular Medicine and Pediatrics, University of California San Diego, La Jolla, CA, USA

Genome-wide association studies (GWAS) in model organisms such as heterogeneous stock (HS) rats provide a valuable complement to human GWAS and offer a unique advantage by enabling the validation of associations through direct experimental manipulations, shedding light on new biological mechanisms. However, determining the causal genes underlying a GWAS signal remains challenging. Most GWAS studies focus on single nucleotide polymorphisms (SNPs) but overlook complex variants such as structural variants (SVs). SVs are longer genome alterations compared to SNPs, which makes them hard to detect with short-read sequencing. By utilizing cutting-edge long reads sequencing technology, our study discovered thousands of SVs in the HS rat population and unravels the role of SVs in their gene expression traits. This will later serve as the basis for SVs imputation for over 20,000 outbred HS rats for which we have extensive drug-abuse related behavioral traits. Our ultimate objective is to uncover novel genetic mechanisms influencing addiction-related behaviors using HS rats.