

Name: Yanchao Pan
PI Name: Hao Chen

Email: hanyou@umich.edu
PI email: hchen@uthsc.edu

**A revamped rat reference genome improves the
discovery of genetic diversity of laboratory rats**

Yanchao Pan¹, Tristan V. de Jong², Panjun Kim², Huda Akil¹, Laura Saba³,
Francesca Telese⁴, Abraham A Palmer⁴, Robert W Williams², Jun Z Li¹,
Hao Chen² on behalf of the International Rat Omics Consortium

¹University of Michigan, ²University Tennessee Health Science Center, ³University of Colorado
Anschutz Medical Campus, ⁴University of California San Diego,

For over a decade, a large research community has relied on a defective assembly of the genome of *Rattus norvegicus* known as Rnor_6.0. The seventh assembly of the rat reference genome—mRatBN7.2, based on the inbred Brown Norway rat, corrects numerous misplaced segments, reduces base-level errors by approximately 9-fold, and increases contiguity by 290-fold, despite having some remaining regions of potential misassembly. Gene annotations are now more complete, leading to significantly improved mapping precision of genomic, transcriptomic and proteomics data sets. Based on this new reference, we evaluated genomic diversity of laboratory rats by conducting a joint analysis of 163 whole genome sequencing data, representing 109 strains/substrains, and defined 15.8 M sites of sequence variation, of which 13.2 K are predicted to have a potential functional impact on 4,407 genes. Phylogenetic analysis confirms and refines the ancestral relationship of these strains. Ten million polymorphisms segregate in the widely used heterogeneous stock rat population, and 8–9 M variants segregate in the HXB/BXH and FXLE/LEXF recombinant inbred families. Some inbred strains differ only by 1–2 M variants, and closely related substrains segregate even fewer. Our analysis also generated a new rat genetic map based on data from 1,893 heterogenous stock rats and provided annotation for transcription start sites and alternative polyadenylation sites. In sum, our updated data and analyses using mRatBN7.2 provide crucial resources for studies using *Rattus norvegicus*.