

Genome-wide association of adiposity in heterogeneous stock rats

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Obesity arises from a complex interaction between genetic and environmental factors, yet the specific genes involved remain largely unidentified. In an initial genome-wide association study (GWAS) using 3,173 outbred N/NIH heterogeneous stock (HS) rats, we identified 32 independent loci associated with obesity-related traits, such as body weight, body length, BMI, fasting glucose, and fat pad weights. Notably, several loci contained a single gene (e.g., *Epha5*, *Nrg1*, *Klhl14*) or other clear candidate genes (e.g., *Adcy3*, *Prhr*), providing strong targets for functional studies.

The initial study, involving 3,173 rats, represented the largest rat GWAS that we are aware of. Our current analysis includes a significantly expanded sample size of 8,857 rats, with 37 quantitative trait loci (QTLs) identified for body weight (SNP heritability: 0.37 ± 0.02). This expanded dataset allows for a more precise understanding of the genetic factors influencing obesity. Additionally, we are further increasing our sample size to over 9,000 rats, specifically focusing on body weight. This substantial increase in sample size enables us to conduct sex-specific analyses, offering deeper insights into the genetic architecture of obesity.

This work underscores the importance of large, well-characterized populations in elucidating the genetic basis of complex traits and highlights the HS rat as a valuable model for obesity research.