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Abstract

Genetic mapping on fully sequenced individuals is transforming understanding of the relationship between molecular variation and variation in complex traits. Here we report a combined sequence and genetic mapping analysis in outbred rats that maps 355 quantitative trait loci for 122 phenotypes. We identify 35 causal genes involved in 31 phenotypes, implicating new genes in models of anxiety, heart disease and multiple sclerosis. The relationship between sequence and genetic variation is unexpectedly complex: at approximately 40% of quantitative trait loci, a single sequence variant cannot account for the phenotypic effect. Using comparable sequence and mapping data from mice, we show that the extent and spatial pattern of variation in inbred rats differ substantially from those of inbred mice and that the genetic variants in orthologous genes rarely contribute to the same phenotype in both species.