Gene Networks and Type 2 Diabetes

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Although >80% of people with type 2 diabetes are obese, most people who are obese do not develop diabetes. We have reproduced this dichotomy in mice by studying two mouse strains that when made obese, differ in diabetes susceptibility. We have mapped diabetes susceptibility loci in an F2 derived from these two strains. We have identified genes that are involved in both insulin signaling and in pancreatic beta cell function. In addition to genetically mapping physiological traits, we also map mRNA abundance as a quantitative trait and thereby define the genetic architecture of gene expression in the context of obesity and diabetes. Using this genetic architecture, we construct causal networks linking gene loci with mRNAs in distinct pathways leading to clinical outcomes.