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Integrating Genetic and Functional Genomic Data to Elucidate Common Disease Tra

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The reconstruction of genetic networks in mammalian systems is one of the primary goals in biological research, especially as such reconstructions relate to elucidating not only common, polygenic human diseases, but living systems more generally. Here I present a statistical procedure for inferring causal relationships between gene expression traits and more classic clinical traits, including complex disease traits. This procedure has been generalized to the gene network reconstruction problem, where naturally occurring genetic variations in segregating mouse populations are used as a source of perturbations to elucidate tissue-specific gene networks. Differences in the extent of genetic control between genders and among four different tissues are highlighted. I also demonstrate that the networks derived from expression data in segregating mouse populations using the novel network reconstruction algorithm are able to capture causal associations between genes that result in increased predictive power, compared to more classically reconstructed networks derived from the same data. This approach to causal inference in large segregating mouse populations over multiple tissues not only elucidates fundamental aspects of transcriptional control, it also allows for the objective identification of key drivers of common human diseases.