Bringing genomic data into focus for studying complex diseases in specific biological contexts

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Overview

Tissue-specific networks are powerful tools for studying complex diseases like autism spectrum disorder (ASD).

We present the first \textbf{genome-wide prediction of autism-associated genes} in the context of the human brain-specific gene network.

The genome-wide predictions, associated brain developmental signatures, functional modules, and prioritized copy-number-variants (CNVs) are all available at asd.princeton.edu.

Studying autism genetics in the context of the human brain

1. Evidence-weighted gold-standard
2. Brain-specific functional gene interaction network
3. Network-based evidence-weighted disease-gene classifier
4. Genotype-wide autism gene prediction
5. Genetic, Developmental, Functional insights

Spatiotemporal developmental expression of autism genes
Brain-specific network-based autism functional modules
Autism CNV gene prioritization and functional characterization

Our ASD-gene predictions are based on a machine learning approach that (1) uses a gold-standard of known disease genes – those linked to autism with varying levels of evidence (E1-4) as positives, and other genes linked to non-neuronal diseases as negatives – in the context of a (2) human brain-specific functional interaction network to (3) build an evidence-weighted network-based classifier capturing autism-specific gene interaction patterns, and (4) predict the level of autism-association of all the genes in the genome. A number of subsequent analyses (5) demonstrate the accuracy and utility of our genome-wide complement of autism-associated genes.