Genomic architecture and gene discovery in autism spectrum disorder

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Autism spectrum disorder (ASD) is characterized by impairments in social communication and restricted or repetitive behavior or interests. Heritability studies demonstrate a high genetic contribution to ASD risk. Advances in genomic technology and statistical methods, along with the availability of large cohorts of ASD families, have revolutionized our understanding of the genomic architecture of ASD and provided a mechanism for robust gene discovery. By integrating new and previously published data from ~2,500 families in the Simons Simplex Collection with published data from the Autism Sequencing Consortium and Autism Genome Project, we identify 71 unique risk loci (6 multigenic loci and 65 genes) associated with ASD based on de novo and rare inherited variants. Phenotypic analysis shows that the de novo mutations are observed more frequently in the presence of female sex, low IQ, or seizures. The 65 risk genes form a cohesive network of protein-protein interactions that is enriched for genes associated with chromatin regulation and synaptic function.

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