Table S1. Validation for the enrichment of ASD genes in this module

	Validation method	Dataset	Conclusion
SFARI-based validation	Comparing with the human synaptome background	synaptomeDB SFARI	Our module is **more enriched** for ASD genes than that of genes in the synaptome background (P=3.28e-8, Fisher's exact test)
	Enrichment of the **non-synaptic** genes in module	synaptomeDB SFARI	Genes in our module **not annotated as synaptic genes** also showed enrichment for ASD genes (P=1.64e-4, hypergeometric test)
	High-confidence loci (with syndromic mutations) and different SFARI versions	SFARI (gene-scoring module, category S)	Significant enrichment (P≤3.85e-06, Fisher's exact)
Independent validation	Enrichment of genes affected by *de novo* ASD disruptive mutations	Sanders, et al; O'Roak, et al.; Neale, et al., 2012, *Nature*	Significant enrichment (P=0.029, Fisher's exact)
	Enrichment of genes affected by *de novo* CNVs in ASD probands	Pinto, et al. 2014, AJHG Sanders et al. and Levy et al. 2011, Neuron	Significant enrichment (P=0.01, Fisher's exact)
	Enrichment of the high-confidence ASD candidate genes with recurrent de novo disruptive mutations	Willsey, A.J. *et al. Cell*, 2014	Significant enrichment (P=3.8e-3, Fisher's exact)
	Enrichment of genes affected by *de novo* CNVs associated with ASD patients	Noh, H.J. et al. PLoS Genet., 2013	Significant enrichment (P=3.1105e-13, Fisher's exact)
	Enrichment of genes affected by rare ASD CNVs	Pinto, D. et al., Nature 2010	Significant enrichment (P=0.0475, Fisher's exact)
	Enrichment of rare nonsynonymous mutations	genome/exome-sequencing in this study	Significant enrichment (P=1.2e-3, hypergeometric test)
	Replication on exome-seq data for >500 patients	Liu, L. et al. PLoS Genet.	Significant overlap with the candidate loci identified in our sequencing study
	1. SynaptomeDB (http://psychiatry.igm.jhmi.edu/SynaptomeDB/) 2. For the comparisons with previously published sequencing dataset, the control gene set includes a set of 9782 genes with indistinguishable CDS length and GC content from the genes in the module. 3. For comparisons involving ASD probands, the same comparisons on unaffected siblisng were also performed.		

Table S1B. Enrichment test for genes with different types of mutations in ASD probands and unaffected siblings					
Test for ASD candidate genes					
CNV test	**module**	**matched control**	**Fold-change**	**P (Fisher's exact)**	**References (PMID)**
de novo CNV (ASD-union, 2753 genes)	19.33%	11.27%	1.7152	0.0124	24768552, 21658581, 21658582
de novo CNV (ASD-intersection, 545 genes)	5.04%	2.07%	2.435	0.0393	24768552, 21658581, 21658582
HC CNV in ASD (203 genes)	14.29%	1.20%	11.91	3.11E-13	23754953
de novo CNV (nonASD, 557 genes)	1.68%	2.65%	0.634	0.7725	21658581, 21658582, 22083728
rare ASD CNV in ASD (407 genes)	5.04%	2.17%	2.3226	0.0475	20531469
de novo SNVs					22495309, 22495306, 22495311
de novo disruptive in proband (67 genes)	2.52%	0.54%	4.67	0.03	
de novo disruptive in siblings (8 genes)	0.00%	0.06%	0	1	
de novo missense in proband (366 genes)	5.04%	2.81%	1.79	0.1543	
de novo missense in siblings (109 genes)	0.84%	0.73%	1.15	0.5826	
de novo silent in proband (148 genes)	0.84%	1%	0.84	1	
de novo silent in siblings (52 genes)	0	0.40%	0	1	
SFARI genes (484 genes)	21%	3.40%	6.18	5.84E-13	https://gene.sfari.org
HC SFARI genes (category S)	5.04%	0.31%	16.26	3.85E-06	

control gene set is matched with CDS length and GC content