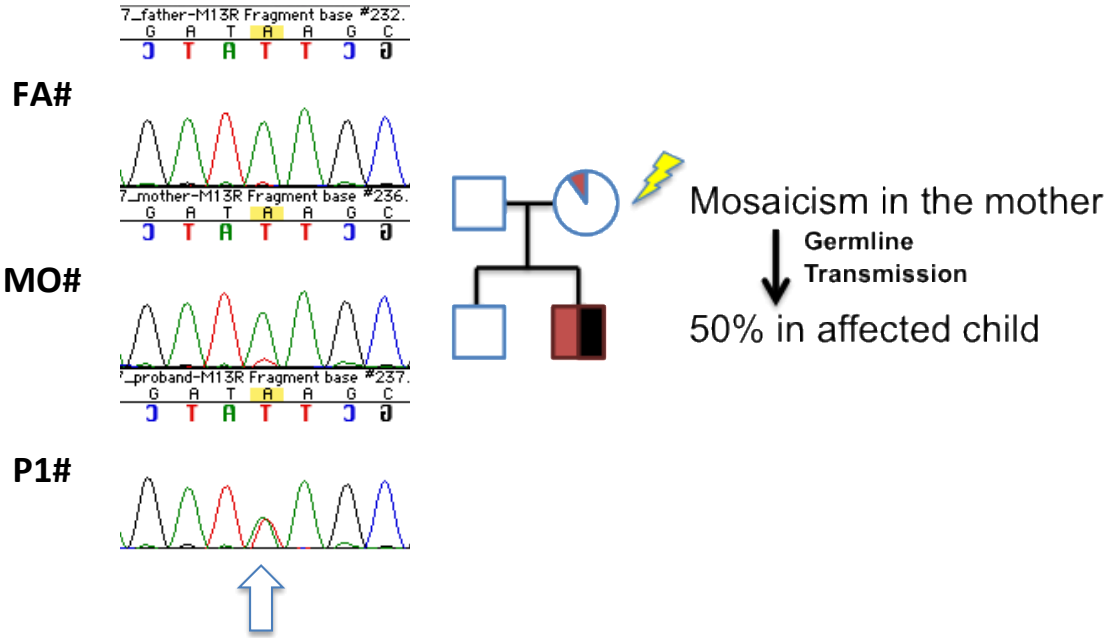
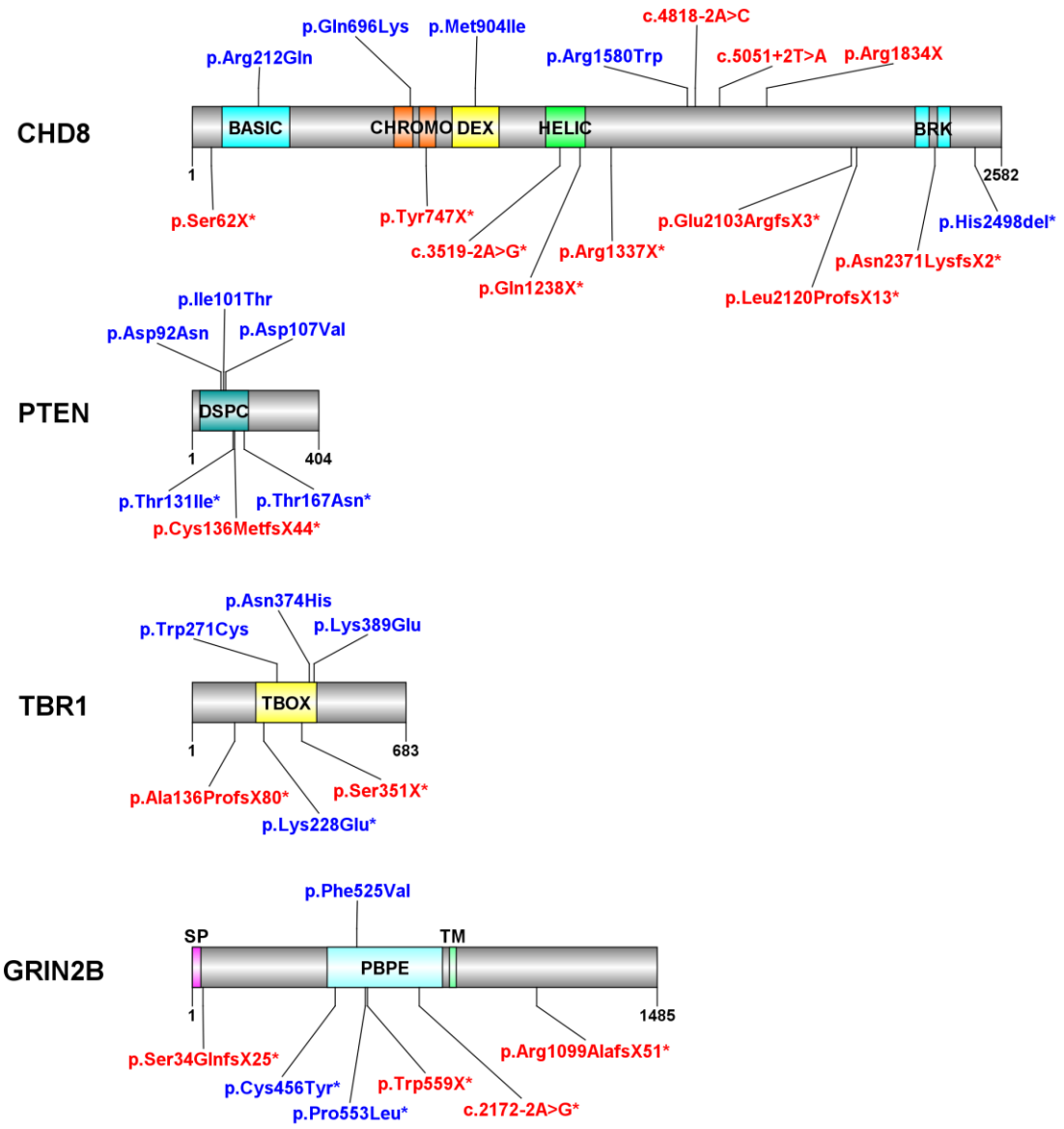
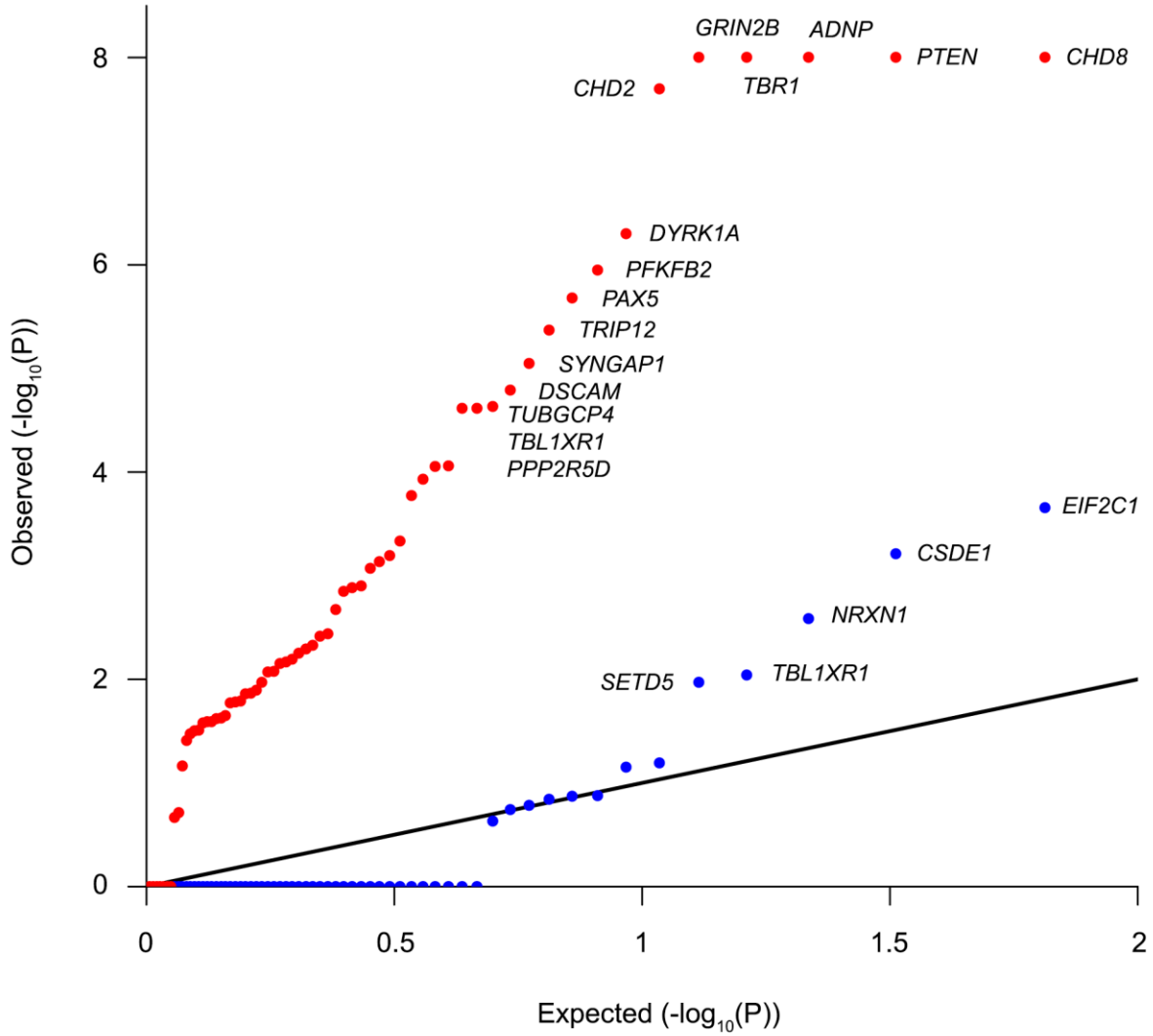


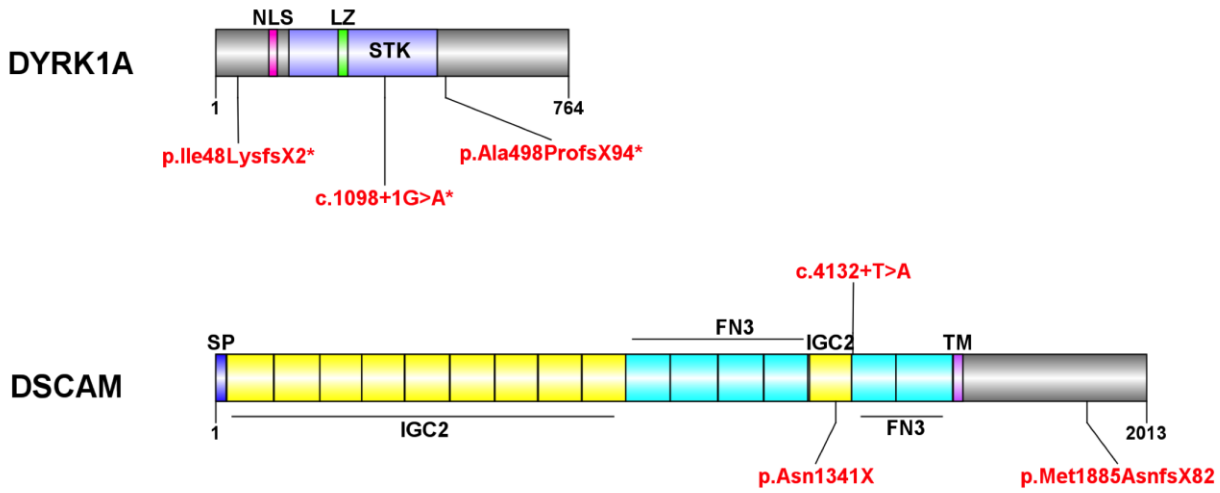
Supplementary Figure 1: Nonsense mutation identified in *ADNP* with smMIPs in the TASC cohort is mosaic in mother.
Left, Sanger traces showing an *ADNP* nonsense mutation (A->T) present at the expected 50:50 ratio in the affected child (P1). smMIPs and the Sanger traces indicate the mother (MO) has the mutation at 10% allele frequency. Right, model of how the mutation arose mosaic in the mother and then was transmitted to affected offspring.



Supplementary Figure 2: Protein diagrams showing *de novo* mutation in four genes previously implicated in ASD.
Protein domains are shown (colored blocks) for the largest protein isoforms as defined by the human protein reference database (HPRD). Mutations shown above the protein structure were newly identified in this study using MIPs. Mutations shown below the protein structure have been previously reported from exome sequencing of ASD/ID cohorts or MIP-based resequencing[1]. Variants followed by an asterisk were reported[1]. Red variants are nonsense, frameshift, or splice site variants and blue variants are missense. Amino acid length is indicated for each protein. Domain abbreviations: CHROMO, chromatin organization modifier; DEX, DEAD-like helicases superfamily; HELIC, helicase superfamily C-terminal; BRK, domain in transcription and CHROMO domain helicases; DSPC, dual specificity protein phosphatase; TBOX, T-box DNA binding; SP, signal peptide; PBPE, eukaryotic homologs of bacterial periplasmic substrate binding proteins; TM, transmembrane.

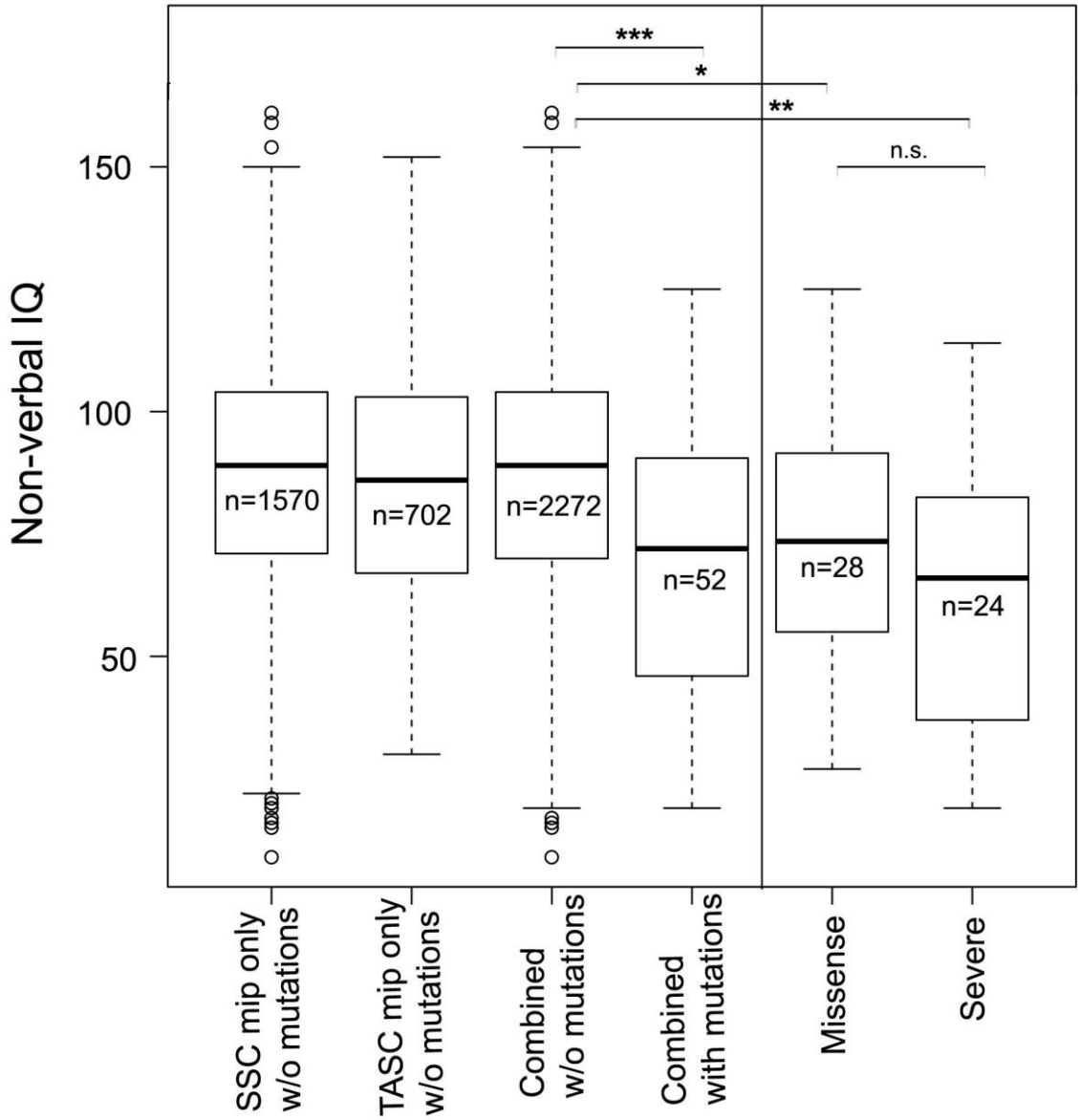


Supplementary Figure 3: Quantile-Quantile plot comparing proband (red) and sibling (blue) mutation simulation results from the ASD MIP plus exome combined data to a uniform distribution.
Addition of exome sequencing data from 1,308 probands (1,157 ASD and 151 ID) and 803 unaffected controls highlights additional genes approaching significance that were not identified from MIP assay alone (**Fig. 1b**). Note: Only a single mutation was observed for *PFKFB2*.



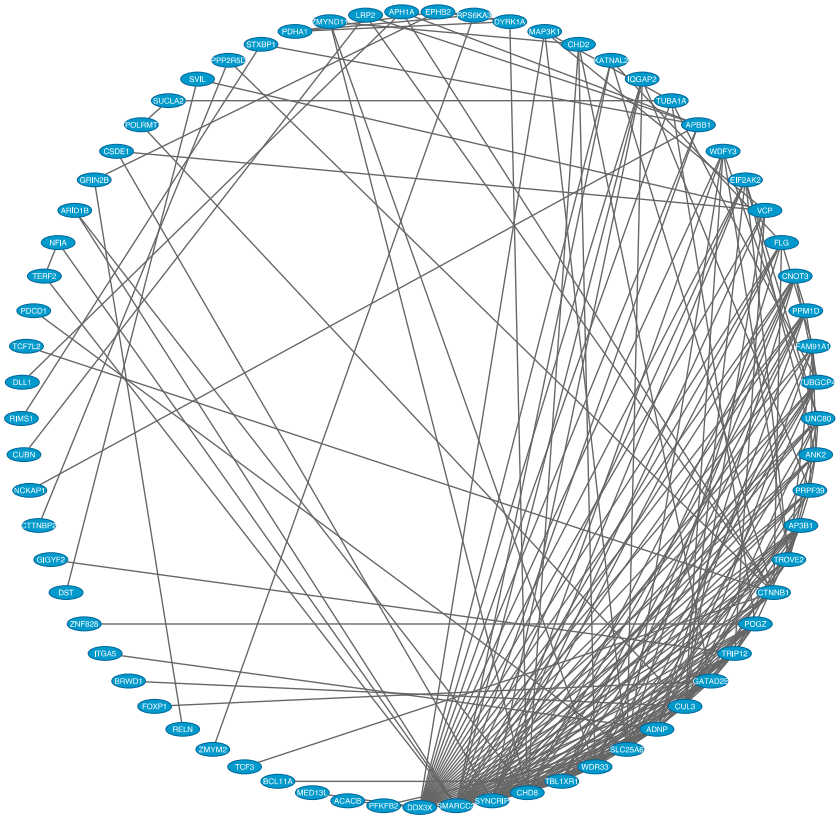
Supplementary Figure 4: Protein diagrams showing *de novo* mutation in ASD probands from two genes, *DYRK1A* and *DSCAM*, from Down syndrome critical regions.

Protein domains are shown (colored blocks) for the largest protein isoforms as defined by HPRD. Mutations shown above the protein structure were newly identified in this study using MIPs. Mutations shown below the protein structure have been previously reported from exome sequencing of ASD/ID cohorts or MIP-based resequencing[1]. Variants followed by an asterisk were reported[1]. Red variants are nonsense, indel, or splice site variants and blue variants are missense. Amino acid length is indicated for each protein. Domain abbreviations: NLS, nuclear localization signal; LZ, leucine zipper; STK, serine-threonine kinase catalytic; SP, signal peptide; IGC2, immunoglobulin C-2 type; FN3, fibronectin type III; TM, transmembrane.



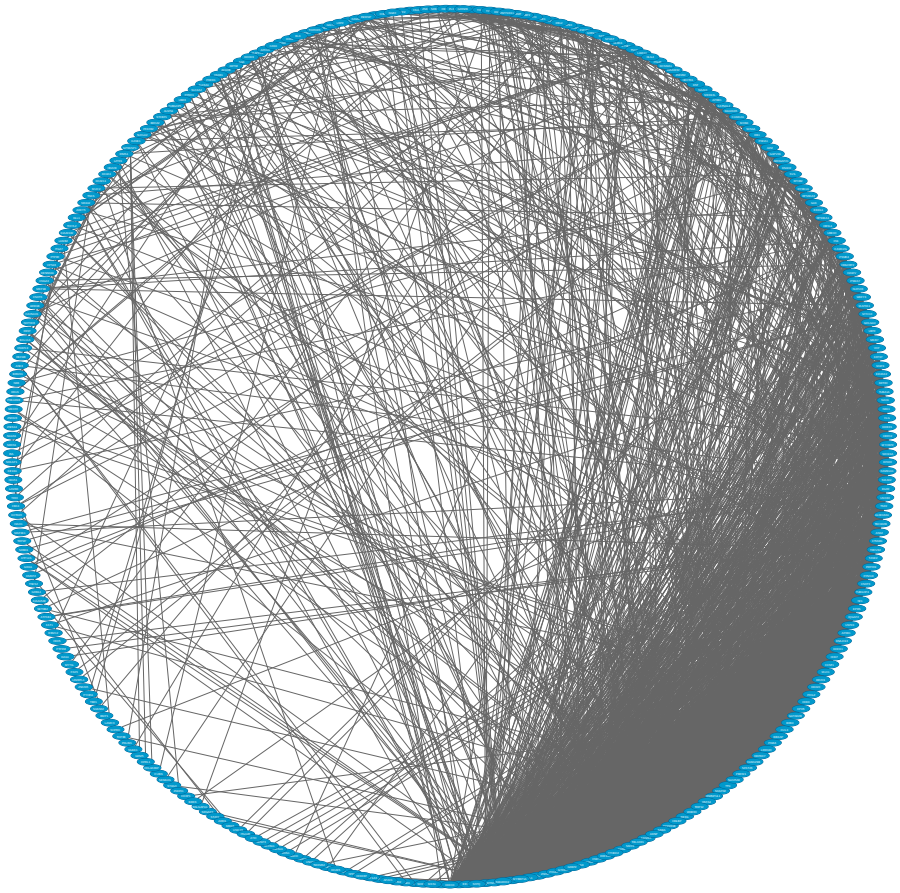
Supplementary Figure 5. IQ comparison of mutation positive and negative samples.

Box and whisker plots of non-verbal IQ scores in probands from both the SSC and TASC cohorts and combined without mutations compared to those probands with mutations identified in this study. Proband mutations have been further divided into severe (indel, splice site, and nonsense) and missense events. Significance was calculated by Wilcox test (two-tailed). *p < 0.05; **p < 1e-03; ***p < 1e-04; n.s. = not significant. Mean/median for groups: SSC w/o: 85.6/89, TASC w/o: 84.6/86, Combined w/o: 85.3/89, Combined w/: 69.2/72, Missense: 74.36/73.5, Severe: 63.2/66.

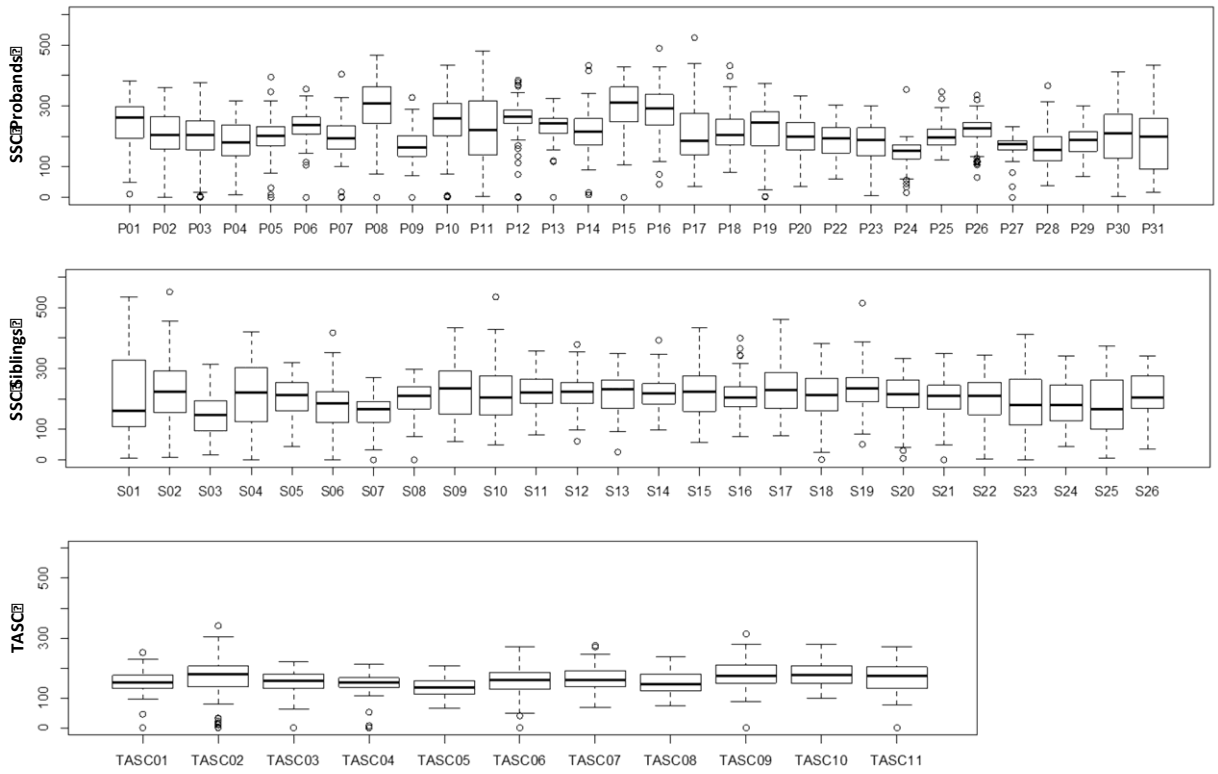


Supplementary Figure 6: Protein-protein interaction (PPI) network of genes with truncating (nonsense, frameshift, splice site) mutations formed from published and unpublished exome data.

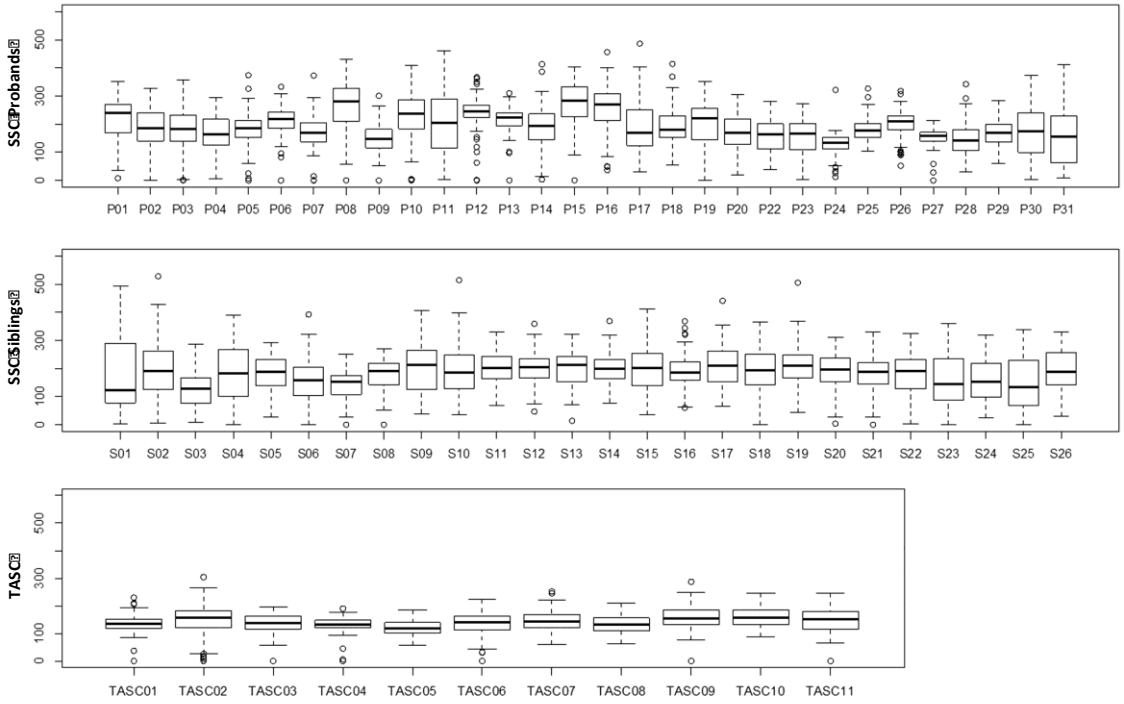
Figure shows interaction network created using the truncating (nonsense, frameshift, splice site) discovery dataset (Methods). Nodes (genes/proteins) are blue ovals. Gray lines represent reported PPI.



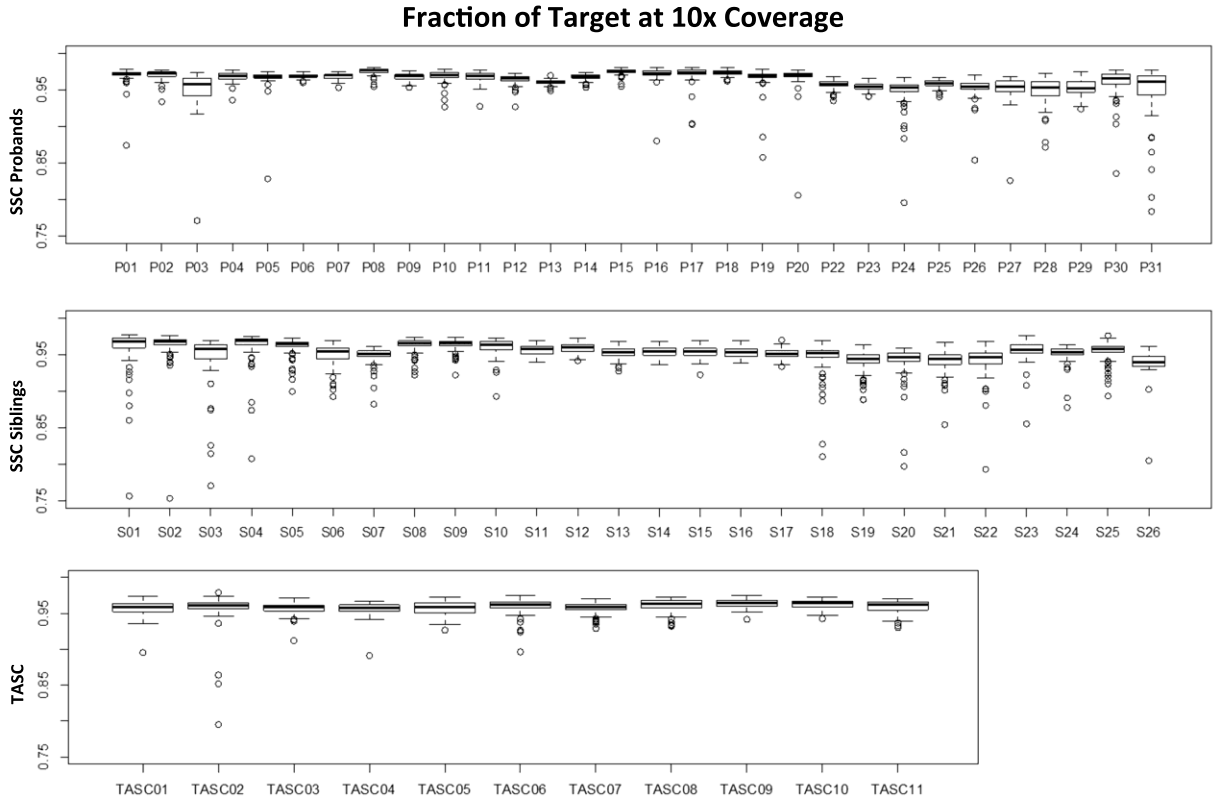
Supplementary Figure 7: Protein-protein interaction (PPI) network of genes with severe missense or truncating mutations formed from published and unpublished exome data.
Figure shows interaction network created using the severe missense or truncating mutations discovery dataset (Methods). Nodes (genes/proteins) are blue ovals. Gray lines represent reported PPI.



Supplementary Figure 8: Mean target coverage across capture plates.
Box and whisker plots showing the mean target coverage across capture plates. Each plot represents one capture plate (~96 samples/plate). All capture samples included (including QC failures).

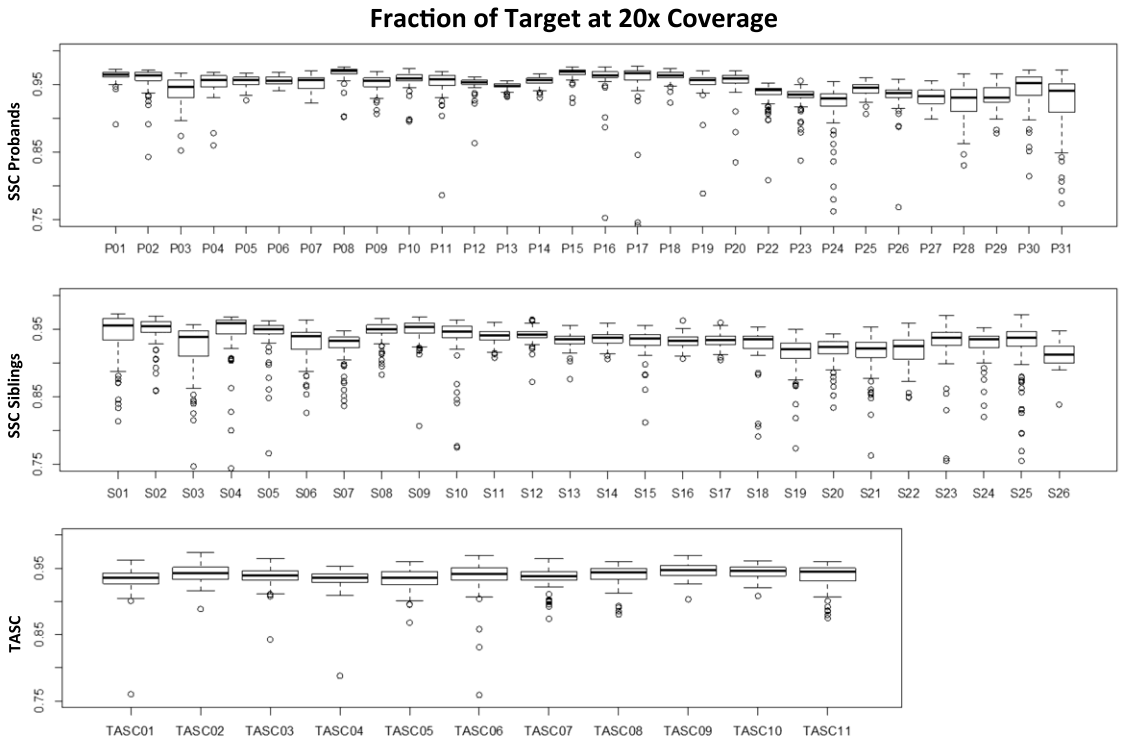


Supplementary Figure 9: Median target coverage across capture plates.
Box and whisker plots showing the median target coverage across capture plates. Each plot represents one capture plate (~96 samples/plate). All capture samples included (including QC failures).



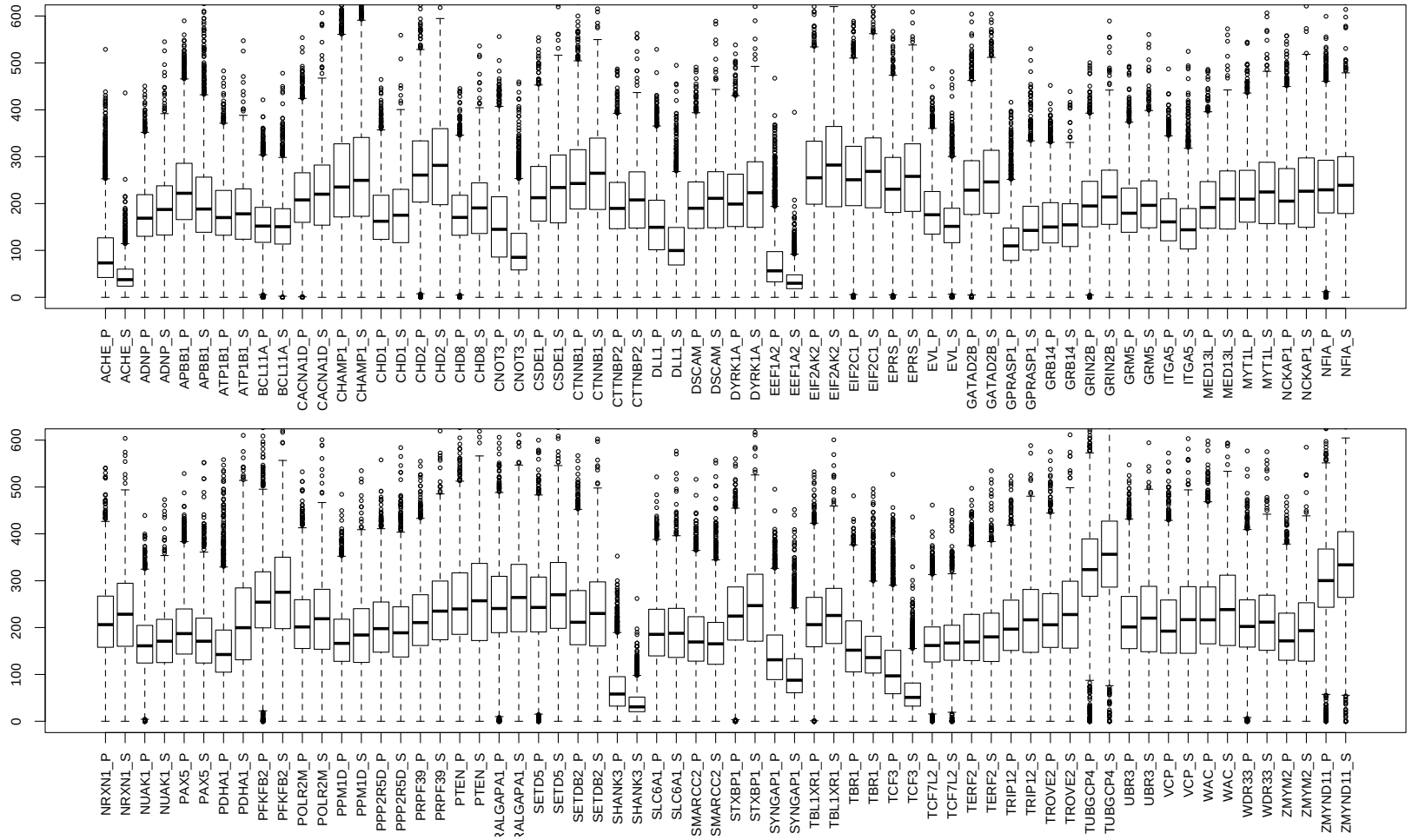
Supplementary Figure 10: Fraction of target based at 10X or greater coverage across capture plates.

Box and whisker plots showing the fraction of a samples target bases at 10X or greater coverage across capture plates. Each plot represents one capture plate (~96 samples/plate). All capture samples included (including QC failures).

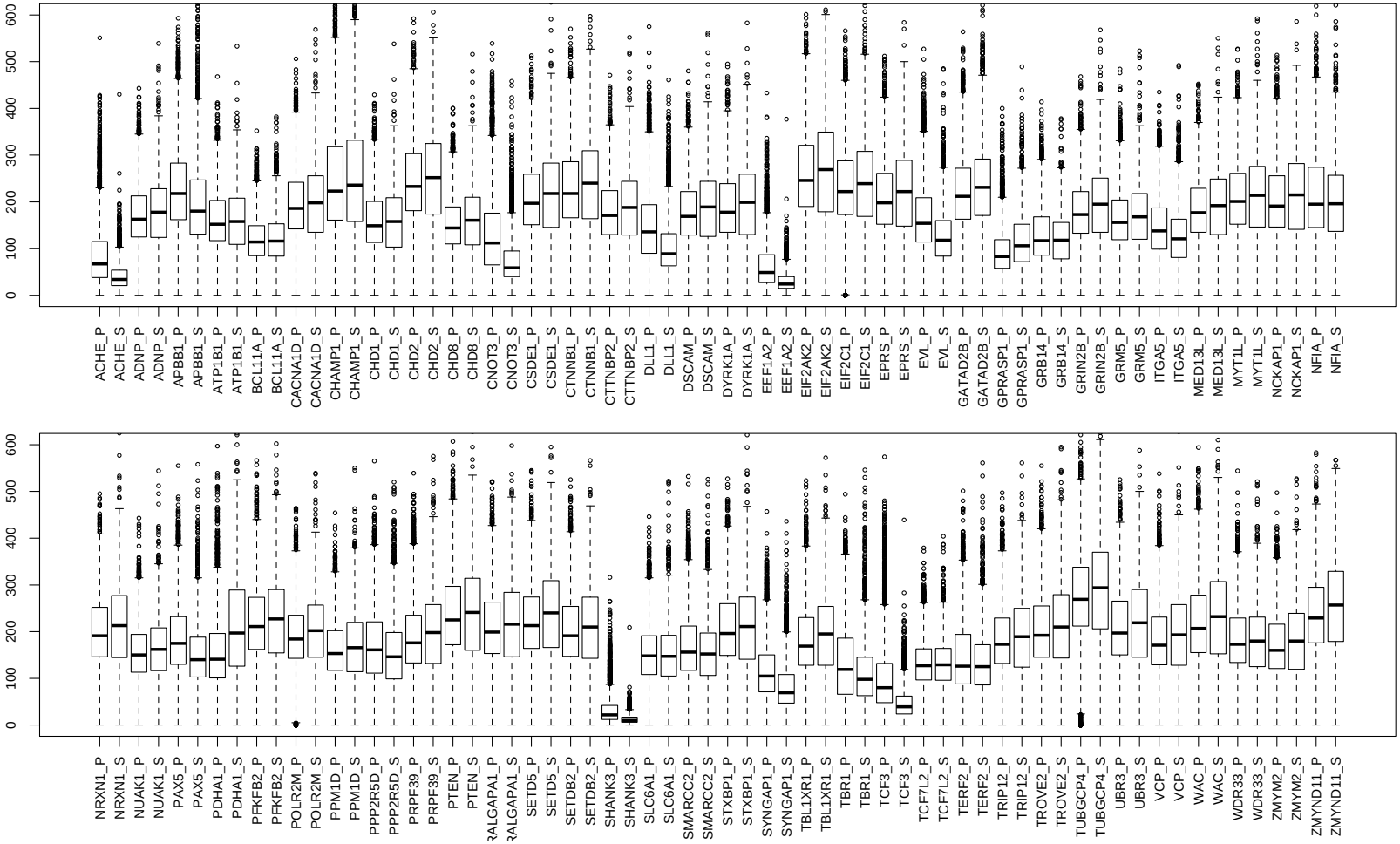


Supplementary Figure 11: Fraction of target based at 20X or greater coverage across capture plates.

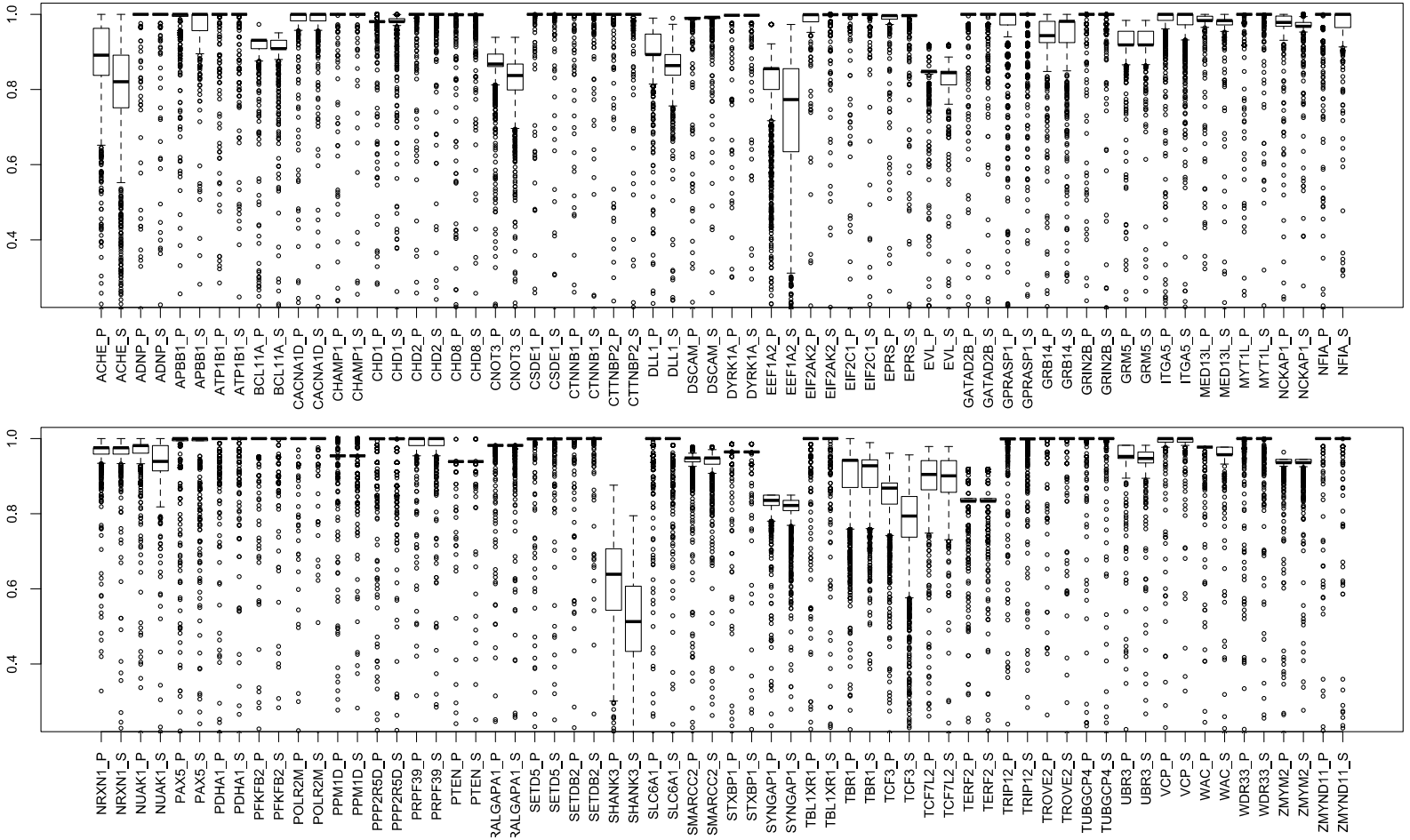
Box and whisker plots showing the fraction of a samples target bases at 20X or greater coverage across capture plates. Each plot represents one capture plate (~96 samples/plate). All capture samples included (including QC failures).



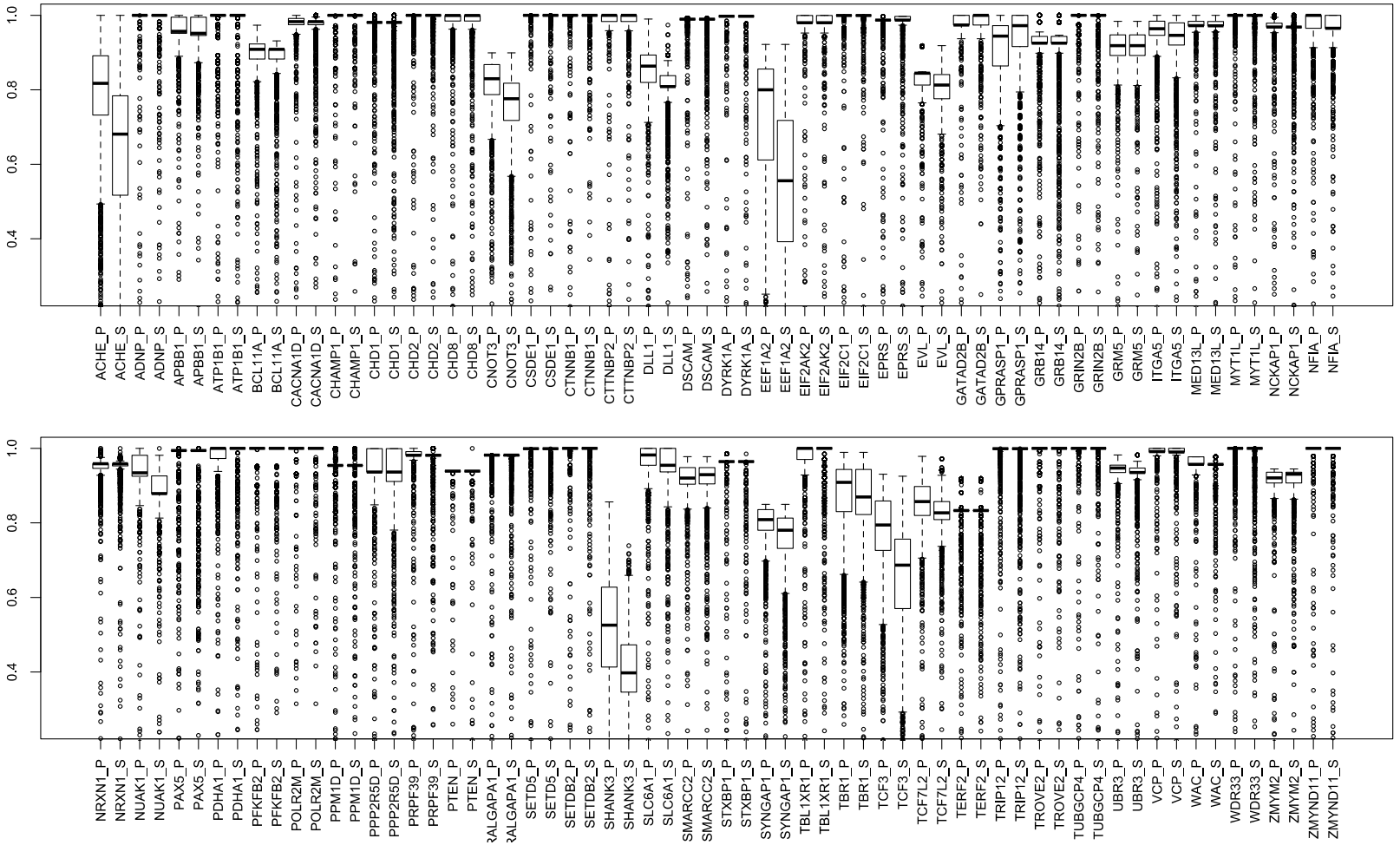
Supplementary Figure 12. Mean target coverage by gene.
Box and whisker plots showing the mean target coverage split by gene. Each plot represents either probands (P) or siblings (S). All capture samples included (including QC failures).



Supplementary Figure 13. Median target coverage by gene.
Box and whisker plots showing the median target coverage split by gene. Each plot represents either probands (P) or siblings (S). All capture samples included (including QC failures).



Supplementary Figure 14. Fraction of target based at 10X or greater coverage by gene.
Box and whisker plots showing the fraction of a samples target bases at 10X or greater coverage split by gene. Each plot represents either probands (P) or siblings (S). All capture samples included (including QC failures).



Supplementary Figure 15. Fraction of target based at 20X or greater coverage by gene.
Box and whisker plots showing the fraction of a samples target bases at 20X or greater coverage split by gene. Each plot represents either probands (P) or siblings (S). All capture samples included (including QC failures).

Supplementary Table 1: Summary of selection of 64 genes for MIP resequencing.

Gene	Selection Summary	Nominating Event(s)		
		Truncating/ Splice	Missense	3n indel
ACHE	Multiple events-missense	0	2	0
ADNP	Top gene in previous study	1	0	0
APBB1	Single events-Network Trunc	1	0	0
ATP1B1	Single events-Network Severe	1	0	0
BCL11A	Single events-Network Trunc	1	0	0
CACNA1D	Multiple events-missense	0	2	0
CHD1	Multiple events-Network Severe	1	1	0
CHD2	Multiple events-Network Trunc	1	1	0
CHD8	Top gene in previous study	3	0	0
CNOT3	Single events-Network Trunc	1	0	0
CSDE1	Single events-Network Trunc	1	0	0
CTNNB1	Top gene in previous study	1	1	0
CTTNBP2	Multiple events-Network Trunc	1	1	0
DLL1	Single events-Network Trunc	1	0	0
DSCAM	Multiple events-Trunc	2	0	0
DYRK1A	Top gene in previous study	2	0	0
EEF1A2	Multiple events-Network Severe	0	2	0
EIF2AK2	Single events-Network Trunc	1	0	0
EIF2C1/AGO1	Multiple events-Network Severe	0	2	0
EPRS	Single events-Network Severe	0	0	1
EVL	Single events-Network Severe	0	0	1*
GATAD2B	Single events-Network Trunc	1	0	0
GPRASP1	Multiple events-Network Severe	0	2	0
GRB14	Single events-Network Severe	1	0	0
GRIN2B	Top gene in previous study	1	1	0
GRINL1A/POLR2M	Single events-Network Severe	0	0	1
GRM5	Single events-Network Severe	0	0	1
ITGA5	Single events-Network Trunc	1	0	0
MED13L	Single events-Network Trunc	1	0	0
MYT1L	Single events-Network Severe	1	0	0
NCKAP1	Single events-Network Trunc	1	0	0
NFIA	Single events-Network Trunc	1	0	0
NRXN1	Single events-Network Severe	1	0	0
NUAK1	Multiple events-Network Severe	1	1	0
PAX5	Single events-Network Severe	1	0	0
PDHA1	Single events-Network Trunc	1	0	0
PFKFB2	Single events-Network Trunc	1	0	0
PPM1D	Single events-Network Trunc	1	0	0
PPP2R5D	Multiple events-Network Trunc	1	1	0
PRPF39	Single events-Network Trunc	1	0	0
PTEN	Top gene in previous study	0	1	0
RALGAPA1	Single events-Network Severe	0	0	1
SETD5	Multiple events-Trunc/severe missense	1	2	0
SETDB2	Single events-Network Severe	1	0	0
SHANK3	Candidate from CNV studies	NA	NA	NA
SLC6A1	Multiple events-Network Severe	1	1	0
SMARCC2	Single events-Network Trunc	1	0	0
STXBP1	Multiple events-Network Trunc	1	3	0
SYNGAP1	Top ID gene	3	0	0

Gene	Selection Summary	Nominating Event(s)		
		Truncating/ Splice	Missense	3n indel
TBL1XR1	Top gene in previous study	1	1	0
TBR1	Top gene in previous study	1	1	0
TCF3	Single events-Network Trunc	1	0	0
TCF7L2	Single events-Network Trunc	1	0	0
TERF2	Single events-Network Trunc	1	0	0
TRIP12	Single events-Network Trunc	1	0	0
TROVE2	Single events-Network Trunc	1	0	0
TUBGCP4	Single events-Network Trunc	1	0	0
UBR3	Single events-Network Severe	1	0	0
VCP	Single events-Network Trunc	1	0	0
WAC	Multiple events-chromatin function	2	0	0
WDR33	Single events-Network Trunc	1	0	0
ZMYM2	Single events-Network Trunc	1	0	0
ZMYND11	Single events-Network Trunc	1	0	0
ZNF828/CHAMP1	Single events-Network Trunc	1	0	0

Network Trunc=gene was present in connected component of PPI network formed from only the truncating/splice exome events. Network Severe=gene was present in connected component of PPI network formed from the truncating/splice and severe missense exome events. Top gene in previous study=One of eight genes sequenced previously.

Supplementary Table 2: Summary of ASD cohorts used for MIP resequencing.

	Captured		Passed QC		Total Passed QC
MIP only	**SSC***	**TASC**	**SSC***	**TASC**	
Probands	1,673	921	1,629	898	2,527
Siblings	1,638	124	1,612	121	1,733
MIP+exome					
Probands	974	NA	959	NA	959
Siblings	773	NA	760	NA	760
Total MIP					
Probands	2,647	921	2,588	898	**3,486**
Siblings	2,411	124	2,372	121	**2,493**

*MIP-only data includes Simons Simplex and Twin Collections. SSC and TASC probands meet ASD criteria on both the ADI-R and ADOS.

Supplementary Table 3: Summary of MIP and MIP plus exome rate comparisons between ASD probands and unaffected siblings.

	MIP Only	Pro	Sib		MIP + ASD exome*	Pro	Sib	
	missense	**30**	**12**		**missense**	**50**	**15**	
	severe	**26**	**2**		**severe**	**81**	**2**	
	n=	2,527	1,733		**n=**	3,681	2,516	
mut rate/child	**any**	0.0222	0.0081		**any**	0.0356	0.0068	
	missense	0.0119	0.0069		**missense**	0.0136	0.0060	
	severe	0.0103	0.0012		**severe**	0.0220	0.0008	
		ratio	**95%CI**	**p-value**		**ratio**	**95%CI**	**p-value**
rate ratios (Pro vs. Sib, one-sided)	**any**	2.74	1.64-Inf	1.99E-04	**any**	5.27	3.40-Inf	5.35E-15
	missense	1.71	0.94-Inf	7.29E-02	**missense**	2.28	1.37-Inf	2.30E-03
	severe	8.92	2.61-Inf	8.83E-05	**severe**	27.68	8.56-Inf	8.83E-05
differential (Pro vs. Sib, one-sided)	**missense**	0.0049			**missense**	0.0076		
	severe	0.0091			**severe**	0.0212		
	total	0.0141			**total**	0.0288		

*Includes all MIP data and ASD exome data.

Supplementary Table 4: Simulation results for MIP-only sequencing data.

Probands	Missense	Severe	P[#]
Total	30	26	0
CHD8	4	7	0
PTEN	4	1	0
ADNP	0	3	1.00E-07
CHD2	0	3	1.00E-06
TBR1	3	0	9.90E-06
GRIN2B	2	1	0.0001174
TRIP12	2	1	0.0001212
SYNGAP1	1	2	0.0001796
PAX5	1	1	0.0002373
NRXN1	1	1	0.0031269
SLC6A1	2	0	0.0063568
CTNNB1	0	1	0.0084704
TUBGCP4	1	0	0.0095999
PPP2R5D	1	0	0.0097979
TCF7L2	0	1	0.01052
NCKAP1	0	1	0.012543
NFIA	1	0	0.0191913
MED13L	0	1	0.0207703
CNOT3	0	1	0.0245474
DSCAM	0	1	0.0312938
WDR33	1	0	0.0758597
VCP	1	0	0.144508
TERF2	1	0	0.147342
MYT1L	1	0	0.153356
EPRS	1	0	0.163572
CHD1	1	0	0.164426
SHANK3	1	0	0.38481
ACHE	0	0	1
APBB1	0	0	1
ATP1B1	0	0	1
BCL11A	0	0	1
CACNA1D	0	0	1
CSDE1	0	0	1

Probands	Missense	Severe	P[#]
CTTNBP2	0	0	1
DLL1	0	0	1
DYRK1A	0	0	1
EEF1A2	0	0	1
EIF2AK2	0	0	1
EIF2C1	0	0	1
GATAD2B	0	0	1
GPRASP1	0	0	1
GRB14	0	0	1
POLR2M	0	0	1
GRM5	0	0	1
ITGA5	0	0	1
NUAK1	0	0	1
PDHA1	0	0	1
PFKFB2	0	0	1
PPM1D	0	0	1
PRPF39	0	0	1
RALGAPA1	0	0	1
SETD5	0	0	1
SETDB2	0	0	1
SMARCC2	0	0	1
STXBP1	0	0	1
TBL1XR1	0	0	1
TCF3	0	0	1
TROVE2	0	0	1
UBR3	0	0	1
WAC	0	0	1
ZMYM2	0	0	1
ZMYND11	0	0	1
CHAMP1	0	0	1
EVL	0	0	1

[#]p-value for observing X or more total protein-altering events, and among them Y or more severe (trunc) events in 10 million simulations.

Siblings	Missense	Severe	P[#]
Total	12	2	0.0003969
EIF2C1	1	1	0.0001254
NRXN1	1	1	0.0015149
SETD5	2	0	0.0061507
TBL1XR1	1	0	0.0067834
CSDE1	1	0	0.0265506
EVL	1	0	0.048238
SETDB2	1	0	0.0530024
VCP	1	0	0.101565
RALGAPA1	1	0	0.102358
MED13L	1	0	0.12598
CNOT3	1	0	0.139651
ACHE	0	0	1
ADNP	0	0	1
APBB1	0	0	1
ATP1B1	0	0	1
BCL11A	0	0	1
CACNA1D	0	0	1
CHD1	0	0	1
CHD2	0	0	1
CHD8	0	0	1
CTNNB1	0	0	1
CTTNBP2	0	0	1
DLL1	0	0	1
DSCAM	0	0	1
DYRK1A	0	0	1
EEF1A2	0	0	1
EIF2AK2	0	0	1
EPRS	0	0	1
GATAD2B	0	0	1
GPRASP1	0	0	1
GRB14	0	0	1
GRIN2B	0	0	1
POLR2M	0	0	1
GRM5	0	0	1
ITGA5	0	0	1
MYT1L	0	0	1
NCKAP1	0	0	1
NFIA	0	0	1
NUAK1	0	0	1
PAX5	0	0	1
PDHA1	0	0	1
PFKFB2	0	0	1
PPM1D	0	0	1
PPP2R5D	0	0	1
PRPF39	0	0	1
PTEN	0	0	1
SLC6A1	0	0	1
SMARCC2	0	0	1
STXBP1	0	0	1
SYNGAP1	0	0	1
TBR1	0	0	1
TCF3	0	0	1
TCF7L2	0	0	1
TERF2	0	0	1
TRIP12	0	0	1
TROVE2	0	0	1
TUBGCP4	0	0	1
UBR3	0	0	1
WAC	0	0	1
WDR33	0	0	1
ZMYM2	0	0	1
ZMYND11	0	0	1
CHAMP1	0	0	1
SHANK3	0	0	1

[#]p-value for observing X or more total protein-altering events, and among them Y or more severe (trunc) events in 10 million simulations.

Supplementary Table 5: Simulation results for MIP and exome combined sequencing data.

Probands	Missense	Severe	P[#]
Total	50	81	0
ADNP	0	4	0
CHD8	4	12	0
PTEN	5	1	0
TBR1	4	2	0
GRIN2B	2	3	1.00E-08
CHD2	1	4	2.00E-08
DYRK1A	0	3	5.00E-07
PFKFB2*	0	1	1.12E-06
PAX5	1	2	2.09E-06
TRIP12	2	2	4.24E-06
SYNGAP1	1	3	8.99E-06
DSCAM	0	3	1.61E-05
TUBGCP4	1	1	2.34E-05
TBL1XR1	1	1	2.42E-05
PPP2R5D	1	1	2.42E-05
NFIA	1	1	8.68E-05
NRXN1	1	2	8.86E-05
TCF7L2	0	2	0.00011715
NCKAP1	0	2	0.00016825
MED13L	0	2	0.0004619
CNOT3	0	2	0.00064021
SLC6A1	3	0	0.00073446
CHD1	2	1	0.00084469
CTNNB1	1	1	0.00125088
WDR33	1	1	0.00130642
NUAK1	1	1	0.00141348
ACHE	2	0	0.00210789
STXBP1	2	0	0.00365712
BCL11A	0	1	0.00381356
VCP	1	1	0.00467812
TERF2	1	1	0.00506048
ZMYND11	0	1	0.00558658
CSDE1	0	1	0.0064307
EPRS	1	1	0.00680074
PRPF39	0	1	0.00700396
TROVE2	0	1	0.00839178
WAC	0	1	0.00848572
GRM5	0	1	0.010621
PPM1D	0	1	0.0127153
APBB1	0	1	0.0135796
ATP1B1	0	1	0.0138053
DLL1	0	1	0.0162043
UBR3	0	1	0.0165419
ZMYM2	0	1	0.01698
CTTNBP2	0	1	0.0223853
SMARCC2	0	1	0.0237569
EIF2AK2	0	1	0.0240092
SETD5	2	0	0.025593
GPRASP1	2	0	0.025718
RALGAPA1	0	1	0.0264834
ITGA5	0	1	0.031027
SHANK3	1	1	0.0311805
CACNA1D	2	0	0.0334055
TCF3	0	1	0.0387885
EIF2C1	1	0	0.0687872
EEF1A2	1	0	0.192735
MYT1L	1	0	0.215197
GATAD2B	0	0	1
GRB14	0	0	1
POLR2M	0	0	1
PDHA1	0	0	1
SETDB2	0	0	1
CHAMP1	0	0	1
EVL	0	0	1

[#]p-value for observing X or more total protein-altering events, and among them Y or more severe (trunc) events in 100 million simulations. *Note only a single event was observed and this gene should not be considered in the significant recurrently mutated gene set.

Siblings	Missense	Severe	P[#]
Total	15	2	0.0003972
EIF2C1	1	1	0.0002206
CSDE1	2	0	0.0006115
NRXN1	1	1	0.0026097
TBL1XR1	1	0	0.0090622
SETD5	2	0	0.0106997
EVL	1	0	0.0638138
SETDB2	1	0	0.069938
VCP	1	0	0.13322
RALGAPA1	1	0	0.134136
GPRASP1	1	0	0.14315
MED13L	1	0	0.164229
CNOT3	1	0	0.181833
DSCAM	1	0	0.234315
ACHE	0	0	1
ADNP	0	0	1
APBB1	0	0	1
ATP1B1	0	0	1
BCL11A	0	0	1
CACNA1D	0	0	1
CHD1	0	0	1
CHD2	0	0	1
CHD8	0	0	1
CTNNB1	0	0	1
CTTNBP2	0	0	1
DLL1	0	0	1
DYRK1A	0	0	1
EEF1A2	0	0	1
EIF2AK2	0	0	1
EPRS	0	0	1
GATAD2B	0	0	1
GRB14	0	0	1
GRIN2B	0	0	1
POLR2M	0	0	1

Siblings	Missense	Severe	P[#]
GRM5	0	0	1
ITGA5	0	0	1
MYT1L	0	0	1
NCKAP1	0	0	1
NFIA	0	0	1
NUAK1	0	0	1
PAX5	0	0	1
PDHA1	0	0	1
PFKFB2	0	0	1
PPM1D	0	0	1
PPP2R5D	0	0	1
PRPF39	0	0	1
PTEN	0	0	1
SLC6A1	0	0	1
SMARCC2	0	0	1
STXBP1	0	0	1
SYNGAP1	0	0	1
TBR1	0	0	1
TCF3	0	0	1
TCF7L2	0	0	1
TERF2	0	0	1
TRIP12	0	0	1
TROVE2	0	0	1
TUBGCP4	0	0	1
UBR3	0	0	1
WAC	0	0	1
WDR33	0	0	1
ZMYM2	0	0	1
ZMYND11	0	0	1
CHAMP1	0	0	1
SHANK3	0	0	1

[#]p-value for observing X or more total protein-altering events, and among them Y or more severe (trunc) events in 10 million simulations.

Supplementary Table 6: Major component nodes and number of edges from PPI network analysis of genes with truncating (nonsense, frameshift, splice site) mutations formed from published and unpublished exome data.

Ensembl_ID	HUGO_ID	#Edges
ENSG00000215301	DDX3X	32
ENSG00000139613	SMARCC2	28
ENSG00000135316	SYNCRIP	23
ENSG00000100888	CHD8	18
ENSG00000136709	WDR33	15
ENSG00000177565	TBL1XR1	15
ENSG00000036257	CUL3	14
ENSG00000101126	ADNP	14
ENSG00000169100	SLC25A6	14
ENSG00000143442	POGZ	12
ENSG00000143614	GATAD2B	12
ENSG00000153827	TRIP12	12
ENSG00000116747	TROVE2	11
ENSG00000168036	CTNNB1	11
ENSG00000132842	AP3B1	10
ENSG00000137822	TUBGCP4	9
ENSG00000144406	UNC80	9
ENSG00000145362	ANK2	9
ENSG00000185246	PRPF39	9
ENSG00000088038	CNOT3	8
ENSG00000170836	PPM1D	8
ENSG00000176853	FAM91A1	8
ENSG00000055332	EIF2AK2	7
ENSG00000143631	FLG	7
ENSG00000165280	VCP	7
ENSG00000163625	WDFY3	6
ENSG00000166313	APBB1	6
ENSG00000145703	IQGAP2	5
ENSG00000167552	TUBA1A	5
ENSG00000095015	MAP3K1	4
ENSG00000133216	EPHB2	4
ENSG00000157540	DYRK1A	4
ENSG00000167216	KATNAL2	4
ENSG00000173575	CHD2	4
ENSG00000177189	RPS6KA3	4
ENSG00000015171	ZMYND11	3
ENSG00000081479	LRP2	3
ENSG00000117362	APH1A	3
ENSG00000131828	PDHA1	3
ENSG00000009307	CSDE1	2
ENSG00000049618	ARID1B	2
ENSG00000099821	POLRMT	2
ENSG00000112640	PPP2R5D	2
ENSG00000132604	TERF2	2
ENSG00000136143	SUCLA2	2
ENSG00000136854	STXBP1	2
ENSG00000150086	GRIN2B	2
ENSG00000162599	NFIA	2
ENSG00000197321	SVIL	2
ENSG00000061676	NCKAP1	1
ENSG00000071564	TCF3	1
ENSG00000076555	ACACB	1
ENSG00000077063	CTTNBP2	1
ENSG00000079841	RIMS1	1
ENSG00000107611	CUBN	1
ENSG00000114861	FOXP1	1
ENSG00000119866	BCL11A	1
ENSG00000121741	ZMYM2	1
ENSG00000123066	MED13L	1
ENSG00000123836	PFKFB2	1
ENSG00000148737	TCF7L2	1
ENSG00000151914	DST	1
ENSG00000161638	ITGA5	1
ENSG00000185658	BRWD1	1
ENSG00000188389	PDCD1	1
ENSG00000189056	RELN	1
ENSG00000198719	DLL1	1
ENSG00000198824	ZNF828	1
ENSG00000204120	GIGYF2	1

Supplementary Table 7: Major component nodes and number of edges from PPI network analysis of genes with severe missense or truncating mutations formed from published and unpublished exome data.

Ensembl_ID	HUGO_ID	#Edges
ENSG00000215301	DDX3X	111
ENSG00000169813	HNRNPF	105
ENSG00000161960	EIF4A1	99
ENSG00000116560	SFPQ	99
ENSG00000175792	RUVBL1	94
ENSG00000139613	SMARCC2	93
ENSG00000197102	DYNC1H1	93
ENSG00000100345	MYH9	93
ENSG00000132382	MYBBP1A	90
ENSG00000151923	TIAL1	83
ENSG00000135316	SYNCRIP	81
ENSG00000075292	ZNF638	78
ENSG00000181222	POLR2A	74
ENSG00000077235	GTF3C1	68
ENSG00000084774	CAD	67
ENSG00000138757	G3BP2	67
ENSG00000141027	NCOR1	65
ENSG00000101210	EEF1A2	64
ENSG00000125107	CNOT1	64
ENSG00000047188	YTHDC2	62
ENSG00000100888	CHD8	61
ENSG00000108055	SMC3	60
ENSG00000004487	KDM1A	59
ENSG00000177565	TBL1XR1	59
ENSG00000101126	ADNP	58
ENSG00000137713	PPP2R1B	57
ENSG00000169375	SIN3A	57
ENSG00000115677	HDLBP	57
ENSG00000130811	EIF3G	56
ENSG00000136709	WDR33	55
ENSG00000153827	TRIP12	54
ENSG00000010292	NCAPD2	53
ENSG00000170606	HSPA4	53
ENSG00000105323	HNRNPUL1	53
ENSG00000163939	PBRM1	52
ENSG00000155657	TTN	52
ENSG00000066557	LRRC40	52
ENSG00000169100	SLC25A6	52
ENSG00000136830	FAM129B	52
ENSG00000121690	DEPDC7	52
ENSG00000145375	SPATA5	52
ENSG00000070061	IKBKAP	48
ENSG00000143870	PDIA6	48
ENSG00000036257	CUL3	47
ENSG00000124571	XPO5	45
ENSG00000141867	BRD4	45
ENSG00000143614	GATAD2B	45
ENSG00000092847	EIF2C1	44
ENSG00000143442	POGZ	44
ENSG00000170004	CHD3	44
ENSG00000064703	DDX20	44
ENSG00000076242	MLH1	43
ENSG00000129315	CCNT1	42
ENSG00000171316	CHD7	41
ENSG00000138246	DNAJC13	41
ENSG00000150760	DOCK1	41
ENSG00000132842	AP3B1	41
ENSG00000162402	USP24	40
ENSG00000145703	IQGAP2	40
ENSG00000136628	EPRS	40
ENSG00000196712	NF1	39
ENSG00000137822	TUBGCP4	39
ENSG00000088038	CNOT3	37
ENSG00000170836	PPM1D	36
ENSG00000116747	TROVE2	35
ENSG00000170921	TANC2	35
ENSG00000185246	PRPF39	35
ENSG00000168036	CTNNB1	33
ENSG00000145362	ANK2	32
ENSG00000059573	ALDH18A1	31
ENSG00000167202	TBC1D2B	31
ENSG00000158526	TSR2	29
ENSG00000144406	UNC80	29
ENSG00000146648	EGFR	29
ENSG00000175387	SMAD2	28
ENSG00000183495	EP400	28

Ensembl_ID	HUGO_ID	#Edges
ENSG00000113615	SEC24A	28
ENSG00000176853	FAM91A1	28
ENSG00000005810	MYCBP2	27
ENSG00000100697	DICER1	26
ENSG00000128731	HERC2	26
ENSG00000143631	FLG	25
ENSG00000137601	NEK1	25
ENSG00000167552	TUBA1A	24
ENSG00000047849	MAP4	24
ENSG00000196531	NACA	24
ENSG00000167767	KRT80	24
ENSG00000055332	EIF2AK2	24
ENSG00000165280	VCP	23
ENSG00000171446	KRT27	23
ENSG00000108312	UBTF	21
ENSG00000148773	MKI67	21
ENSG00000144674	GOLGA4	20
ENSG00000095015	MAP3K1	20
ENSG00000133026	MYH10	20
ENSG00000101182	PSMA7	19
ENSG00000105968	H2AFV	19
ENSG00000069248	NUP133	19
ENSG00000163625	WDFY3	19
ENSG00000167674	HDGFRP2	18
ENSG00000068878	PSME4	18
ENSG00000009335	UBE3C	17
ENSG00000148660	CAMK2G	17
ENSG00000115414	FN1	17
ENSG00000117676	RPS6KA1	16
ENSG00000114867	EIF4G1	16
ENSG00000124006	OBSL1	16
ENSG00000178950	GAK	15
ENSG00000177189	RPS6KA3	14
ENSG00000133216	EPHB2	14
ENSG00000157540	DYRK1A	14
ENSG00000107863	ARHGAP21	13
ENSG00000183914	DNAH2	13
ENSG00000197321	SVIL	13
ENSG00000139687	RB1	12
ENSG00000131828	PDHA1	12
ENSG00000165219	GAPVD1	12
ENSG00000070808	CAMK2A	12

Ensembl_ID	HUGO_ID	#Edges
ENSG00000144285	SCN1A	12
ENSG00000175899	A2M	12
ENSG00000115540	MOB4	12
ENSG00000102030	NAA10	11
ENSG00000166313	APBB1	11
ENSG00000167216	KATNAL2	11
ENSG00000123066	MED13L	11
ENSG00000177728	KIAA0195	11
ENSG00000092148	HECTD1	10
ENSG00000151914	DST	10
ENSG00000161638	ITGA5	9
ENSG00000156113	KCNMA1	9
ENSG00000103197	TSC2	9
ENSG00000091106	NLRC4	9
ENSG00000188994	ZNF292	9
ENSG00000021574	SPAST	9
ENSG00000170871	KIAA0232	9
ENSG00000132535	DLG4	9
ENSG00000131018	SYNE1	9
ENSG00000135862	LAMC1	9
ENSG00000138760	SCARB2	8
ENSG00000121741	ZMYM2	8
ENSG00000124486	USP9X	8
ENSG00000137878	GRINL1A	8
ENSG00000172845	SP3	8
ENSG00000103479	RBL2	8
ENSG00000099821	POLRMT	7
ENSG00000162946	DISC1	7
ENSG00000071564	TCF3	7
ENSG00000102780	DGKH	7
ENSG00000005381	MPO	7
ENSG00000015171	ZMYND11	7
ENSG00000077063	CTTNBP2	7
ENSG00000185024	BRF1	7
ENSG00000162599	NFIA	6
ENSG00000149503	INCENP	6
ENSG00000198911	SREBF2	6
ENSG00000150086	GRIN2B	6
ENSG00000112640	PPP2R5D	6
ENSG00000196628	TCF4	6
ENSG00000189367	C6orf174	6
ENSG00000166147	FBN1	6

Ensembl_ID	HUGO_ID	#Edges
ENSG00000196576	PLXNB2	6
ENSG00000081479	LRP2	6
ENSG00000066248	NGEF	6
ENSG00000183454	GRIN2A	6
ENSG00000132604	TERF2	6
ENSG00000153922	CHD1	6
ENSG00000198026	ZNF335	6
ENSG00000128578	FAM40B	6
ENSG00000080815	PSEN1	6
ENSG00000147044	CASK	5
ENSG00000156711	MAPK13	5
ENSG00000153071	DAB2	5
ENSG00000174672	BRSK2	5
ENSG00000009307	CSDE1	5
ENSG00000006530	AGK	5
ENSG00000135679	MDM2	5
ENSG00000108759	KRT32	5
ENSG00000204120	GIGYF2	5
ENSG00000117362	APH1A	5
ENSG00000197579	TOPORS	5
ENSG00000088387	DOCK9	5
ENSG00000173575	CHD2	5
ENSG00000076555	ACACB	5
ENSG00000136573	BLK	5
ENSG00000136854	STXBP1	4
ENSG00000164889	SLC4A2	4
ENSG00000136143	SUCLA2	4
ENSG00000099949	LZTR1	4
ENSG00000119599	DCAF4	4
ENSG00000188389	PDCD1	4
ENSG00000144357	UBR3	4
ENSG00000116127	ALMS1	4
ENSG00000198932	GPRASP1	4
ENSG00000048052	HDAC9	4
ENSG00000079841	RIMS1	4
ENSG00000153575	TUBGCP5	4
ENSG00000123836	PFKFB2	4
ENSG00000107104	KANK1	4
ENSG00000100897	DCAF11	4
ENSG00000157103	SLC6A1	4
ENSG00000139618	BRCA2	4
ENSG00000148840	PPRC1	4

Ensembl_ID	HUGO_ID	#Edges
ENSG00000144191	CNGA3	3
ENSG00000153234	NR4A2	3
ENSG00000198788	MUC2	3
ENSG00000081248	CACNA1S	3
ENSG00000132004	FBXW9	3
ENSG00000104142	VPS18	3
ENSG00000151150	ANK3	3
ENSG00000148737	TCF7L2	3
ENSG00000173273	TNKS	3
ENSG00000142949	PTPRF	3
ENSG00000113300	CNOT6	3
ENSG00000198719	DLL1	3
ENSG00000119866	BCL11A	3
ENSG00000117859	OSBPL9	3
ENSG00000173175	ADCY5	3
ENSG00000074181	NOTCH3	3
ENSG00000131149	KIAA0182	3
ENSG00000135424	ITGA7	3
ENSG00000141434	MEP1B	3
ENSG00000172037	LAMB2	3
ENSG00000084093	REST	3
ENSG00000174485	DENND4A	3
ENSG00000049618	ARID1B	3
ENSG00000179915	NRXN1	2
ENSG00000075673	ATP12A	2
ENSG00000061676	NCKAP1	2
ENSG00000068784	SRBD1	2
ENSG00000104814	MAP4K1	2
ENSG00000115290	GRB14	2
ENSG00000121621	KIF18A	2
ENSG00000155511	GRIA1	2
ENSG00000144021	CIAO1	2
ENSG00000169760	NLGN1	2
ENSG00000177697	CD151	2
ENSG00000038382	TRIO	2
ENSG00000196405	EVL	2
ENSG00000188191	PRKAR1B	2
ENSG00000112078	KCTD20	2
ENSG00000198824	ZNF828	2
ENSG00000122778	KIAA1549	2
ENSG00000169057	MECP2	2
ENSG00000107854	TNKS2	2

Ensembl_ID	HUGO_ID	#Edges
ENSG00000196878	LAMB3	2
ENSG00000141582	CBX4	2
ENSG00000083857	FAT1	2
ENSG00000010818	HIVEP2	2
ENSG00000143153	ATP1B1	2
ENSG00000122482	ZNF644	2
ENSG00000136169	SETDB2	2
ENSG00000185658	BRWD1	2
ENSG00000183091	NEB	2
ENSG00000092439	TRPM7	2
ENSG00000189056	RELN	2
ENSG00000182791	CCDC87	1
ENSG00000066923	STAG3	1
ENSG00000136535	TBR1	1
ENSG00000011143	MKS1	1
ENSG00000168959	GRM5	1
ENSG00000170581	STAT2	1
ENSG00000186487	MYT1L	1
ENSG00000047936	ROS1	1
ENSG00000139990	DCAF5	1
ENSG00000173276	ZNF295	1
ENSG00000160305	DIP2A	1
ENSG00000113163	COL4A3BP	1
ENSG00000115760	BIRC6	1
ENSG00000137842	TMEM62	1
ENSG00000064999	ANKS1A	1
ENSG00000100038	TOP3B	1
ENSG00000107438	PDLIM1	1
ENSG00000129159	KCNC1	1
ENSG00000107611	CUBN	1
ENSG00000164116	GUCY1A3	1
ENSG00000114861	FOXP1	1
ENSG00000125510	OPRL1	1
ENSG00000095637	SORBS1	1
ENSG00000112200	ZNF451	1

Ensembl_ID	HUGO_ID	#Edges
ENSG00000148053	NTRK2	1
ENSG00000163564	PYHIN1	1
ENSG00000196092	PAX5	1
ENSG00000133958	UNC79	1
ENSG00000138363	ATIC	1
ENSG00000168487	BMP1	1
ENSG00000146414	SHPRH	1
ENSG00000174373	RALGAPA1	1
ENSG00000196220	SRGAP3	1
ENSG00000138685	FGF2	1
ENSG00000166233	ARIH1	1
ENSG00000108861	DUSP3	1
ENSG00000162105	SHANK2	1
ENSG00000179776	CDH5	1
ENSG00000010322	NISCH	1
ENSG00000152284	TCF7L1	1
ENSG00000173482	PTPRM	1
ENSG00000074590	NUAK1	1
ENSG00000136531	SCN2A	1
ENSG00000181555	SETD2	1
ENSG00000050555	LAMC3	1
ENSG00000005961	ITGA2B	1
ENSG00000042781	USH2A	1
ENSG00000151623	NR3C2	1
ENSG00000120868	APAF1	1
ENSG00000244462	RBM12	1
ENSG00000100170	SLC5A1	1
ENSG00000185513	L3MBTL1	1
ENSG00000095539	SEMA4G	1
ENSG00000173402	DAG1	1
ENSG00000204406	MBD5	1
ENSG00000167671	UBXN6	1

Supplementary Reference

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