

## Supplementary Methods

**The sample.** Genotypes from 6709 samples from 10 sites were returned from the Translational

Counts of genotyped DNAs returned from TGEN.										
AGRE	IMGSAC	CPEA	Canada	Stanford	Duke	Vanderbilt	Paris	UNC	Mt. Sinai	Total
2213	1357	937	530	469	344	295	240	236	88	6709

Genomics Research Institute or TGEN. In the received diagnosis file, there was a total of 1496 nominal families (Table 1, manuscript), genotypes from 1491 families were returned by TGEN, and when intersected there were 1317 families with both (useful) genotypes and diagnostic status. Nominal family structures were simple and most consisted of nuclear families ( $\approx 86\%$ ).

### Structure and counts of families.

Diagnostic group	No. marriages	No. families	No. nuclear	marriage/family
Narrow	659	522	450 (0.86)	1.26
Broad	904	731	636 (0.87)	1.24
hASD	507	437	393 (0.90)	1.16

The average number of marriages per family was roughly 1.21.

The distribution of affected pairs is given below as counts of pairs of a specific kind per family, although we note that some of the different relative pairs fall in the same family. Suppose for example, in a participating family there was an affected sibling pair and an affected cousin; this family would contribute 1 to the full sibling pairs (FS) and 2 to cousins (CC) count. In addition, if there were four affected siblings in a single nuclear family, there would be 6 pairs and the family would contribute a count of 1 to the FS column in row 6.

Counts of relative pairs per family.							
pairs	FS	PO	HS	NN	CC	125	OTHER
1	1017	1	17	6	36	5	6
2	3	0	4	1	6	1	0
3	85	0	0	0	2	0	0
4	0	0	0	0	2	0	2
5	0	0	0	0	0	0	0
6	2	0	0	0	0	0	0

FS = Full Sibs; PO = Parent/Offspring; HS = Half Sibs; NN = Uncle/Aunt with Nephew/Niece; CC = First Cousins; 125 = pairs with Kinship Coefficient of .125; and OTH = Pairs with Kinship Coefficient  $< .125$ .

**Power.** Our power estimates integrate results from various sources from the literature (Risch 1990, Krawczak 2001). Roughly, we should have a power of 80% to detect linkage of loci with a stringent LOD score of 3 threshold contributing a locus-specific risk of  $\geq 1.29$  for a sample size of 1,181 ASPs. (Our sample is slightly larger, in the sense that some families are extended.) For a sample of roughly 700 ASP, locus-specific risk of  $\geq 1.54$  is required have a power of 80% to detect linkage; and, for a sample of roughly 400 ASP, locus-specific risk of  $\geq 1.88$  is required.

**Discussion of merging CNV information with linkage data.** Our approach to merging CNV information with linkage data is necessarily limited by the uncertainty inherent in judging CNV-conferred risk. One would like to partition CNVs into known CNAs, those likely to be CNAs,

those unlikely to be CNAs, and those CNVs that are simply polymorphisms unrelated to ASD. In fact, a statistically-efficient linkage analysis would use a continuous scoring system for CNVs, scoring them 0 if they are certain to be a CNA and 1 if they are certain to be only a polymorphism, with intermediate scores reflecting the degree of ASD risk conferred. It would be natural to place the scoring system in a Bayesian framework, in which the prior (a function of the score and confidence in the CNV call) was established by expert opinion. Because the relationship between CNV and CNA is so unclear at the moment, and the grid of markers too sparse for high confidence in CNV calls, we decided to forego such analyses. Nonetheless our rudimentary approach to linkage analysis with data on CNV yields some intriguing results. Linkage statistics in key genomic regions drop for the filtered and plate methods of CNV-calling, but surprisingly often they increase for the batch method. The most conservative explanation for this observation is that the effect of batch is due to chance, while the effect of filtered and plate is due to diminishing sample size. It is also possible, however, that the increased linkage seen with batch results could be meaningful. If they were, then some of the CNVs dropped in batch, but not the other CNV-calling methods, must be particularly salient for risk to autism.

### **Supplementary References**

Risch, N (1990) Linkage strategies for genetically complex traits. II. The power of affected relative pairs. *Am. J. Hum. Genet.* 46: 229-241.

Krawczak, M (2001) ASP – a simulation-based power calculator for genetic linkage studies of qualitative traits, using sib-pairs. *Hum. Genet.* 109:675-677.

**Mapping autism risk loci using genetic linkage and chromosomal rearrangements** (The Autism Genome Project (AGP) Consortium)

**Supplementary Table 1. List of 624 CNVs in Filtered Analysis.**



Sample ID	CNV/sample	Chr	Cytoband	Start	Stop	Size	#SNPs/segment	CNV	Familial	Mendelian error	dGV	RefGene	% overlap
NAAR015-H9-R-103-008	1	2	2q22.3	145,475,000	145,587,000	112,000	3	gain					0.0%
NAAR050-D4-02C11231	1	2	2q23.3\l2q24.1	152,760,000	158,096,000	5,336,000	29	loss					13.2%
NAAR001-A9-8002-202	7	2	2q24.1	154,759,000	155,131,000	372,000	4	loss					0.0%
NAAR071-F2-04C33150	1	2	2q24.1	156,592,000	157,717,000	1,125,000	8	gain					0.0%
NAAR077-H7-05C40979	1	2	2q24.3	165,478,000	166,218,000	740,000	4	gain					0.0%
NAAR048-G6-02C09923	2	2	2q31.1	172,258,000	172,303,000	45,000	3	loss					0.0%
NAAR006-A3-8125-201	6	2	2q32.1	184,270,000	186,428,000	2,158,000	11	gain	yes				14.5%
NAAR006-A4-8125-202	1	2	2q32.1	184,623,000	186,428,000	1,805,000	9	gain	yes				9.2%
NAAR057-F1-H11281	2	2	2q32.1	185,302,000	186,892,000	1,590,000	8	gain					0.0%
NAAR072-A12-H11255	1	2	2q33.3	206,453,000	206,453,000	0	2	loss					0.0%
NAAR072-H7-H11818	2	2	2q35\l2q36.1	216,710,000	222,518,000	5,808,000	19	gain					5.6%
NAAR075-G4-04C36260	1	3	3p26.3	1,100,380	1,167,990	67,610	3	loss					100.0%
NAAR062-A2-H10717	1	3	3p26.3	1,478,480	2,264,800	786,320	6	gain					47.3%
NAAR009-F6-8241-111	1	3	3p25.3	8,379,730	8,917,610	537,880	8	loss					0.0%
NAAR009-F8-8241-202	1	3	3p25.3	8,379,730	8,917,610	537,880	8	loss					0.0%
NAAR027-D4-3118.002	3	3	3p25.2\l3p25.1	12,870,700	13,806,400	935,700	4	gain					39.5%
NAAR058-D6-H11540	6	3	3p14.2	59,347,700	59,711,600	363,900	7	gain					0.0%
NAAR007-B2-8159-101	1	3	3p14.1	67,773,300	68,967,900	1,194,600	7	loss	yes				2.1%
NAAR007-B4-AU32503	1	3	3p14.1	67,773,300	68,967,900	1,194,600	7	loss	yes	yes			2.1%
NAAR007-B6-8159-203	1	3	3p14.1	67,773,300	68,967,900	1,194,600	7	loss	yes	yes			2.1%
NAAR077-H11-H11824	4	3	3p13	70,753,700	71,252,700	499,000	4	gain					0.0%
NAAR030-F9-3192.001	1	3	3p12.2	82,496,200	83,190,200	694,000	6	gain	yes				0.2%
NAAR037-A9-1014-A9-P3	3	3	3p12.2	82,496,200	83,190,200	694,000	6	gain	yes	yes			0.2%
NAAR025-D4-3081.005	1	3	3p12.1	85,618,700	85,619,200	500	3	loss					0.0%
NAAR038-H4-1010-A4-P1	1	3	3p12.1	85,618,700	85,619,200	500	3	loss					0.0%
NAAR076-A7-04C36353	1	3	3p12.1	85,618,700	85,619,200	500	3	loss					0.0%
NAAR078-D11-R-001-017	1	3	3p12.1	85,618,700	85,619,200	500	3	loss					0.0%
NAAR020-F1-H11314	4	3	3p11.1	88,032,900	88,845,400	812,500	3	gain					0.0%
NAAR072-G5-H10615	1	3	3q13.31	117,973,000	118,274,000	301,000	5	loss	yes				0.0%
NAARC2-P2-D11-H10615	1	3	3q13.31	117,973,000	118,274,000	301,000	5	loss	yes				0.0%
NAAR049-E2-02C10442	1	3	3q24	149,082,000	149,082,000	0	2	loss					0.0%
NAAR054-G9-H10354	1	3	3q24	149,082,000	149,082,000	0	2	loss					0.0%
NAAR064-F5-H12040	5	3	3q25.1\l3q25.2	152,567,000	154,110,000	1,543,000	8	gain					39.2%
NAAR007-F6-8177-202	3	3	3q25.31\l3q25.32	157,517,000	159,424,000	1,907,000	10	gain					8.6%
NAAR064-F12-H12093	5	3	3q25.31\l3q25.32	157,517,000	158,701,000	1,184,000	7	gain					10.8%
NAAR045-E11-01C07334	1	3	3q25.33\l3q26.1	160,960,000	162,570,000	1,610,000	7	gain					1.8%
NAAR035-G7-1014-G7-P1	2	3	3q26.1	163,337,000	163,337,000	0	2	gain					0.0%
NAAR017-A10-T-006-0001	1	3	3q28\l3q29	193,786,000	195,272,000	1,486,000	12	loss					36.4%
NAAR059-C9-H11878	1	3	3q29	196,940,000	197,775,000	835,000	2	gain					100.0%
NAAR051-C4-H12583	1	4	4p16.3	398,952	3,565,630	3,166,678	4	gain					21.2%
NAAR052-F6-H10682	3	4	4p16.3\l4p16.2\l4p16.1'	398,952	17,044,800	16,645,848	64	loss					25.0%
NAAR062-H3-H11083	2	4	4p16.3\l4p16.2\l4p16.1	398,952	6,790,030	6,391,078	12	gain					27.6%
NAAR071-B8-H13174	2	4	4p15.33\l4p16.1	10,760,900	11,857,300	1,096,400	7	gain					1.0%
NAAR052-F6-H10682	3	4	4p15.32\l4p15.31\l4p15	18,188,800	23,734,200	5,545,500	20	loss					17.3%
NAAR035-C8-1014-C8-P1	1	4	4p15.2	24,846,300	24,846,500	200	2	gain					0.0%
NAAR045-G12-POS	4	4	4p15.2\l4p15.1	27,420,500	28,639,200	1,218,700	8	gain	yes				24.9%
NAAR054-G12-POS	1	4	4p15.1	28,022,000	31,238,500	3,216,500	12	gain	yes				25.1%
NAAR065-F7-H12361	3	4	4p15.1	28,022,000	28,870,800	848,800	7	gain					37.3%
NAAR065-G7-H11752	8	4	4p15.1	28,022,000	28,639,200	617,200	6	gain					48.4%
NAAR049-B1-02C10026	2	4	4p15.1	28,415,900	28,639,200	223,300	5	gain					46.3%
NAAR041-G3-01C05464	1	4	4p14	36,753,900	36,754,600	700	2	loss					0.0%
NAAR047-C1-01C08451	2	4	4p14	36,753,900	36,754,600	700	2	loss					0.0%
NAAR071-F10-04C33160	1	4	4p14	36,753,900	36,754,600	700	2	loss					0.0%
NAAR074-G9-04C35936	1	4	4p14	36,753,900	36,754,600	700	2	loss					0.0%
NAAR033-C1-3257.002	1	4	4q13.3	71,219,300	71,371,300	152,000	4	loss	yes				0.0%
NAAR033-E1-3257.005	1	4	4q13.3	71,219,300	71,371,300	152,000	4	loss	yes	yes			0.0%
NAAR001-A9-8002-202	7	4	4q13.3	71,370,900	71,371,300	400	3	loss					0.0%
NAAR072-D11-04C34503	1	4	4q13.3	71,370,900	71,371,300	400	3	gain					0.0%
NAAR066-A3-H10147	1	4	4q21.22	83,267,800	83,268,300	500	2	loss					0.0%
NAAR010-F6-8268-111	1	4	4q26	116,524,000	118,226,000	1,702,000	9	gain	yes				18.1%
NAAR010-F7-8268-201	1	4	4q26	117,347,000	118,226,000	879,000	7	gain	yes				11.2%
NAAR015-E3-F-022-002	1	4	4q28.1	127,566,000	128,446,000	880,000	8	gain					0.0%
NAAR061-D2-H10427	2	4	4q32.2	164,134,000	164,820,000	686,000	3	gain					0.4%
NAAR069-F6-H12662	2	4	4q32.2\l4q32.3	164,134,000	167,151,000	3,017,000	15	gain					5.9%
NAAR044-H2-01C06588	1	4	4q34.1	173,117,000	173,653,000	536,000	6	gain					0.3%
NAAR014-E1-1999227	1	4	4q34.2\l4q34.3	177,732,000	178,003,000	271,000	6	gain					0.0%
NAAR047-C1-01C08451	2	4	4q34.3	179,062,000	179,589,000	527,000	5	gain					0.0%
NAAR046-F3-01C08055	2	4	4q34.3\l4q35.1\l4q35.2	182,216,000	188,232,000	6,016,000	27	gain					11.6%
NAAR010-E5-8265-111	1	4	4q34.3	182,703,000	182,703,000	0	3	gain					0.0%
NAAR031-C8-3213.002	1	4	4q34.3	182,703,000	182,703,000	0	3	gain					0.0%
NAAR033-E7-3271.001	3	4	4q34.3	182,703,000	182,703,000	0	3	loss					0.0%
NAAR047-F7-01C08499	1	4	4q35.1\l4q35.2	185,809,000	189,310,000	3,501,000	17	gain	yes				14.9%
NAAR047-F8-01C08500	1	4	4q35.1\l4q35.2	185,809,000	189,310,000	3,501,000	17	gain	yes				14.9%
NAAR047-F9-01C08501	1	4	4q35.1\l4q35.2	185,809,000	189,310,000	3,501,000	17	gain	yes				14.9%
NAAR062-D5-H10869	1	4	4q35.2	188,796,000	189,905,000	1,109,000	10	gain	yes				29.4%
NAAR062-D6-H10890	1	4	4q35.2	188,901,000	189,905,000	1,004,000	9	gain	yes				32.5%
NAAR062-D7-H10891	1	4	4q35.2	188,901,000	189,310,000	409,000	4	loss	yes				0.0%
NAAR006-A6-8126-101	1	4	4q35.2	189,303,000	189,310,000	7,000	3	loss					0.0%













**Mapping autism risk loci using genetic linkage and chromosomal rearrangements** (The Autism Genome Project (AGP) Consortium)

**Supplementary Table 2. List of 254 CNVs in Affected Individuals.**







Sample ID	CNV/sample	Chr	Cytoband	Start	Stop	Size	#SNPs/segment	CNV	Familial	Mendelian error	dGV	RefGene	% overlap
NAAR017-D4-HI2243	1	16	16q23.3	81,327,500	82,050,200	722,700	5	gain					0.0%
NAAR068-B12-HI1404	2	17	17p12	14,304,400	15,237,700	933,300	10	gain	yes				0.0%
NAAR001-E1-8012-201	1	17	17p12	14,432,900	15,237,700	804,800	9	loss	yes	yes			0.7%
NAAR045-A5-01C06730	3	17	17p12	14,691,500	15,108,700	417,200	4	gain				ACOXL NM_018308 tBCL2L11 NM_138624 tBCL2L11 NM_138621 tBCL2L	100.0%
NAAR003-A5-8047-202	4	17	17q21.1 17q25.2 17t	33,248,900	76,399,500	43,150,600	88	gain		yes			0.0%
NAAR067-D12-HI2767	2	18	18p11.32	1,564,270	1,964,310	400,040	10	gain	yes				69.2%
NAAR076-D4-04C36611	1	18	18p11.32	1,748,000	1,807,190	59,190	4	loss					0.0%
NAAR022-A10-3023.004	1	18	18p11.21 18p11.22	10,741,600	11,601,400	859,800	7	gain	yes			SUCLG2 NM_003848 tFAM19A4 NM_001005527 tFAM19A1 NM_213609 t	2.1%
NAAR022-H9-3023.003	1	18	18p11.21 18p11.22	10,741,600	11,601,400	859,800	7	gain	yes			FOXB1 NM_012182	0.0%
NAAR001-F11-8017-202	3	18	18p11.21	11,554,300	11,601,400	47,100	3	loss				PMP22 NM_153322 tPMP22 NM_003041 tTEKT3 NM_031898 tFLJ45831	100.0%
NAAR036-E10-1014-E10-P2	3	18	18q11.2	18,307,400	18,529,700	222,300	4	gain				CAPZA3 NM_03328 tPLCZ1 NM_033123 tPIK3C2G NM_004570 tAEBP2	2.5%
NAAR050-H11-HI2539	2	18	18q11.2	18,307,400	18,529,700	222,300	4	gain				GAB2 NM_012296 tGAB2 NM_080491	0.0%
NAAR058-D6-HI1540	6	18	18q11.2	18,307,400	18,529,700	222,300	4	gain				PMP22 NM_153322 tFLJ45831 NM_001001684 tTEKT3 NM_031898 tPMPF	100.0%
NAAR036-B11-1014-B11-P2	1	18	18q12.2 18q12.3	34,993,000	35,619,700	626,700	5	loss	yes	yes		KRTAP19-4 NM_181610 tKRTAP19-6 NM_181612 tKRTAP19-5 NM_1816	0.0%
NAAR020-B4-HI0937	1	19	19q12	32,869,600	33,398,500	528,900	7	gain				ATP5J NM_001003696 tCRYZL1 NM_145858 tCLDN14 NM_144492 tC21c	10.8%
NAAR071-F1-04C33149	1	19	19q13.11	37,946,700	39,375,900	1,429,200	8	gain					0.3%
NAAR041-G7-01C05468	2	20	20p13	95,685	691,220	595,535	4	gain	yes				100.0%
NAAR041-A2-99C00465	4	20	20q13.33	59,180,200	59,682,100	501,900	5	gain				SLC27A4 NM_005094 tC5 NM_001735 tCDK9 NM_001261 tRAPGEF1 NM	11.0%
NAAR010-H3-8273-202	1	21	21q11.2	13,520,500	13,574,800	54,300	2	gain					100.0%
NAAR017-C2-HI2202	1	21	21q22.11	30,538,900	30,983,100	444,200	8	gain	yes			C2orf10 NM_194250	9.2%
NAAR069-A4-HI2923	1	21	21q22.3	46,751,900	46,782,200	30,300	2	gain					6.8%
NAAR030-C8-3183.007	1	22	22q11.21	17,506,900	19,774,000	2,267,100	4	loss					18.1%
NAAR063-B1-HI1183_2	2	22	22q11.21	17,506,900	20,306,800	2,799,900	5	gain	yes			NDUFA11 NM_175614 tZNF441 NM_152355 tTICAM1 NM_182919 tFLJ90	10.2%
NAAR074-A11-04C35671	2	22	22q12.1	26,638,100	27,802,400	1,164,300	4	gain					0.0%
NAAR001-G4-8018-201	1	22	22q13.32 22q13.33	47,765,700	48,006,700	241,000	3	loss				GAB2 NM_080491 tGAB2 NM_012296	0.0%
NAAR053-F1-03C15328	1	22	22q13.32 22q13.33	48,004,600	48,881,300	876,700	4	loss	yes	yes			19.2%
NAAR072-F11-200501053	3	22	22q13.32 22q13.33	48,004,600	48,881,300	876,700	4	loss	yes	yes			19.2%
NAAR002-B3-8026-204	2	22	22q13.33	48,881,000	48,881,300	300	2	gain					100.0%

**Mapping autism risk loci using genetic linkage and chromosomal rearrangements** (The Autism Genome Project (AGP) Consortium)

**Supplementary Table 3. Breakdown of CNVs in Affected Individuals.**

Supplementary Table 6: Breakdown of CNVs in Affected Individuals (NCBI Build 35)

CNVs Overlapping with Autsim Chromosomal Rearrangement Database							
Sample ID	CNV/sample	Chr	Start	Stop	Size	#SNPs/segment	CNV
NAAR052-F6-HI0682	3	4	398,952	17,044,800	16,645,848	64	loss
NAAR003-A5-8047-202	4	5	9,538,490	16,046,000	6,507,510	24	loss
NAAR078-A3-200305415	9	6	104,688,000	112,813,000	8,125,000	29	gain
NAAR059-G5-HI2100	1	7	87,837,300	89,132,500	1,295,200	6	gain
NAAR062-H3-HI1083	2	8	1,130,900	6,780,950	5,650,050	32	loss
NAAR002-B3-8026-204	2	15	21,490,300	22,083,700	593,400	9	gain
NAAR024-B7-3064.003	1	15	21,490,300	25,698,400	4,208,100	18	gain
NAAR024-C7-3064.004	1	15	21,490,300	25,698,400	4,208,100	18	gain
NAAR039-C9-1021-C9-P3	2	15	21,490,300	25,698,400	4,208,100	18	gain
NAAR039-E9-1012-F2-PA	1	15	21,490,300	25,698,400	4,208,100	18	gain
NAAR065-E6-HI0302	1	15	21,490,300	25,698,400	4,208,100	18	gain
NAAR065-E7-HI0304	1	15	21,490,300	25,698,400	4,208,100	18	gain
NAAR015-C12-F-016-003	1	15	21,885,600	22,083,700	198,100	6	gain
NAAR052-E6-HI0308	1	15	23,325,300	24,495,700	1,170,400	4	gain
NAAR078-A3-200305415	9	15	49,345,700	100,170,000	50,824,300	190	gain
NAAR055-A4-HI0442	2	15	74,290,400	100,170,000	25,879,600	104	gain
NAAR030-C8-3183.007	1	22	17,506,900	19,774,000	2,267,100	4	loss
NAAR063-B1-HI1183_2	2	22	17,506,900	20,306,800	2,799,900	5	gain
Recurrent CNVs							
Sample ID	CNV/sample	Chr	Start	Stop	Size	#SNPs/segment	CNV
NAAR007-D6-8172-202	1	1	143,780,000	144,894,000	1,114,000	7	gain
NAAR048-G5-02C09922	1	1	143,780,000	144,894,000	1,114,000	7	gain
NAAR007-D5-8172-201	1	1	143,780,000	144,894,000	1,114,000	7	gain
NAAR003-F10-8064-201	1	2	88,993,300	88,993,400	100	2	loss
NAAR003-A5-8047-202	4	2	88,993,300	88,993,400	100	2	loss
NAAR025-D4-3081.005	1	3	85,618,700	85,619,200	500	3	loss
NAAR078-D11-R-001-017	1	3	85,618,700	85,619,200	500	3	loss
NAAR027-C6-3120.003	1	4	189,303,000	189,310,000	7,000	3	loss
NAAR071-A7-HI3161	1	4	189,303,000	189,310,000	7,000	3	loss
NAAR056-B12-HI0790	1	4	189,303,000	189,310,000	7,000	3	loss
NAAR070-H5-HI3148	1	4	189,303,000	189,310,000	7,000	3	loss
NAAR007-A6-8156-201	1	4	189,303,000	189,310,000	7,000	3	loss
NAAR027-D6-3120.004	1	4	189,303,000	189,310,000	7,000	3	loss
NAAR030-F12-3198.004	2	5	29,073,500	29,136,100	62,600	4	loss
NAAR050-H5-HI2533	2	5	29,073,500	29,136,100	62,600	4	loss
NAAR030-E12-3198.003	1	5	29,073,500	29,136,100	62,600	4	loss
NAAR046-D1-01C08018	1	5	75,136,400	75,136,700	300	3	loss
NAAR031-G8-3214.004	1	5	75,136,400	75,136,700	300	3	loss
NAAR069-F6-HI2662	2	8	142,072,000	142,072,000	0	2	gain
NAAR077-C8-04C37826	1	8	142,072,000	142,072,000	0	2	gain
NAAR027-A12-3129.004	1	9	239,391	1,599,250	1,359,859	8	gain
NAAR065-B12-HI2269	3	9	239,391	1,599,250	1,359,859	8	gain
NAAR069-H9-04C29142	3	9	38,017,600	38,288,600	271,000	4	gain
NAAR037-A9-1014-A9-P3	3	9	38,017,600	38,288,600	271,000	4	gain
NAAR057-F1-HI1281	2	10	92,008,800	93,008,000	999,200	7	gain
NAAR047-H1-02C09502	8	10	92,008,800	93,008,000	999,200	7	gain
NAAR076-G5-04C37170	1	11	21,709,100	21,709,300	200	3	gain
NAAR076-G4-04C37169	1	11	21,709,100	21,709,300	200	3	gain
NAAR056-C2-HI0799	1	11	50,096,900	50,595,000	498,100	6	gain
NAAR068-F2-HI2862	2	11	50,096,900	50,595,000	498,100	6	gain
NAAR001-A9-8002-202	7	11	50,418,000	50,595,000	177,000	3	loss
NAAR020-F12-HI1566	3	11	50,418,000	50,595,000	177,000	3	loss
NAAR051-G1-HI2618	1	13	22,502,100	23,692,300	1,190,200	9	gain
NAAR041-F10-00C04574	2	13	22,502,100	23,692,300	1,190,200	9	gain
NAAR036-E10-1014-E10-P2	3	14	21,305,700	21,719,200	413,500	9	gain
NAAR038-D6-1015-D6-P1	1	14	21,305,700	21,719,200	413,500	9	gain
NAAR065-E7-HI0304	1	15	21,490,300	25,698,400	4,208,100	18	gain
NAAR065-E6-HI0302	1	15	21,490,300	25,698,400	4,208,100	18	gain
NAAR024-B7-3064.003	1	15	21,490,300	25,698,400	4,208,100	18	gain
NAAR039-E9-1012-F2-PA	1	15	21,490,300	25,698,400	4,208,100	18	gain
NAAR024-C7-3064.004	1	15	21,490,300	25,698,400	4,208,100	18	gain
NAAR039-C9-1021-C9-P3	2	15	21,490,300	25,698,400	4,208,100	18	gain
NAAR036-E10-1014-E10-P2	3	18	18,307,400	18,529,700	222,300	4	gain
NAAR050-H11-HI2539	2	18	18,307,400	18,529,700	222,300	4	gain
NAAR058-D6-HI1540	6	18	18,307,400	18,529,700	222,300	4	gain
NAAR072-F11-200501053	3	22	48004600	48881300	876700	4	loss
NAAR053-F1-03C15328	1	22	48004600	48881300	876700	4	loss

Overlapping CNVs								
Sample ID	CNV/sample	Chr	Start	Stop	Size	#SNPs/segment	CNV	
NAAR074-A7-04C35667	5	1	60,389,500	61,350,000	960,500	6	gain	
NAAR074-D1-04C35701	1	1	60,629,100	61,350,000	720,900	5	gain	
NAAR025-E10-3090.002	1	1	143,780,000	144,479,000	699,000	6	gain	
NAAR006-A3-8125-201	6	1	158,901,000	159,090,000	189,000	6	gain	
NAAR069-H9-04C29142	3	1	158,901,000	159,599,000	698,000	7	gain	
NAAR043-F6-01C06146	1	2	1,725,230	1,743,780	18,550	3	gain	
NAAR043-F7-01C06147	1	2	1,725,230	1,743,780	18,550	3	gain	
NAAR006-A3-8125-201	6	2	184,270,000	186,428,000	2,158,000	11	gain	
NAAR006-A4-8125-202	1	2	184,623,000	186,428,000	1,805,000	9	gain	
NAAR057-F1-HI1281	2	2	185,302,000	186,892,000	1,590,000	8	gain	
NAAR007-F6-8177-202	3	3	157,517,000	159,424,000	1,907,000	10	gain	
NAAR064-F12-HI2093	5	3	157,517,000	158,701,000	1,184,000	7	gain	
NAAR046-F3-01C08055	2	4	182,216,000	188,232,000	6,016,000	27	gain	
NAAR031-C8-3213.002	1	4	182,703,000	182,703,000	0	3	gain	
NAAR047-F8-01C08500	1	4	185,809,000	189,310,000	3,501,000	17	gain	
NAAR047-F9-01C08501	1	4	185,809,000	189,310,000	3,501,000	17	gain	
NAAR062-D6-HI0890	1	4	188,901,000	189,905,000	1,004,000	9	gain	
NAAR062-D7-HI0891	1	4	188,901,000	189,310,000	409,000	4	loss	
NAAR023-F9-3046.003	1	4	189,670,000	190,118,000	448,000	7	loss	
NAAR073-E12-04C35554	1	4	189,670,000	190,118,000	448,000	7	gain	
NAAR073-F2-04C35556	1	4	189,670,000	190,200,000	530,000	8	gain	
NAAR024-A12-3072.008	1	4	189,808,000	191,091,000	1,283,000	12	loss	
NAAR041-G7-01C05468	2	4	190,013,000	191,091,000	1,078,000	8	loss	
NAAR046-F3-01C08055	2	4	190,013,000	191,091,000	1,078,000	8	gain	
NAAR003-D6-8056-201	1	5	39,448,600	39,469,900	21,300	2	gain	
NAAR055-A4-HI0442	2	6	3,801,430	18,594,500	14,793,070	67	loss	
NAAR041-A2-99C00465	4	6	77,520,700	78,789,900	1,269,200	8	gain	
NAAR066-F1-HI2710	2	6	78,060,300	79,324,200	1,263,900	9	gain	
NAAR041-A2-99C00465	4	6	104,688,000	105,059,000	371,000	5	gain	
NAAR078-A3-200305415	9	6	104,688,000	112,813,000	8,125,000	29	gain	
NAAR010-G1-B269-202	2	6	165,016,000	165,037,000	21,000	3	loss	
NAAR078-A3-200305415	9	6	165,016,000	167,022,000	2,006,000	13	loss	
NAAR064-H2-HI2133	1	7	12,577,400	12,826,100	248,700	5	gain	
NAAR064-E5-HI1947	1	8	3,909,530	4,949,310	1,039,780	12	gain	
NAAR067-A8-HI2741	2	8	3,909,530	3,909,710	180	2	gain	
NAAR006-F6-8145-201	2	8	4,473,850	5,900,610	1,426,760	13	gain	
NAAR052-F3-HI0633	2	8	104,786,000	142,072,000	37,286,000	139	gain	
NAAR035-G1-1014-G1-P1	1	8	134,743,000	134,743,000	0	2	gain	
NAAR050-H5-HI2533	2	9	239,391	559,992	320,601	5	gain	
NAAR064-F6-HI2067	3	9	239,391	33,916,500	33,677,109	213	gain	
NAAR041-F10-00C04574	2	9	11,611,200	12,277,900	666,700	10	loss	
NAAR065-B12-HI2269	3	9	11,611,200	14,481,300	2,870,100	31	gain	
NAAR052-H6-HI1012	1	9	12,010,900	12,277,900	267,000	6	loss	
NAAR065-B12-HI2269	3	9	28,114,200	31,349,900	3,235,700	11	gain	
NAAR046-H2-01C08084	4	9	111,481,000	111,802,000	321,000	6	gain	
NAAR030-G10-3194.003	1	10	68,424,900	68,552,100	127,200	6	gain	
NAAR077-E7-05C39675	6	10	92,152,400	93,008,000	855,600	5	gain	
NAAR050-H11-HI2539	2	10	127,758,000	127,758,000	0	3	gain	
NAAR068-E11-HI2859	2	11	49,879,900	50,595,000	715,100	7	gain	
NAAR057-E5-HI1258	1	11	113,502,000	134,403,000	20,901,000	95	gain	
NAARCP2-A7-S-082-003	1	11	133,403,000	134,403,000	1,000,000	5	gain	
NAAR035-E11-1014-E11-P1	1	11	134,083,000	134,403,000	320,000	4	gain	
NAAR024-E10-3070.004	1	11	134,394,000	134,403,000	9,000	3	gain	
NAAR060-C5-HI2203	1	12	93,683	130,547,000	130,453,317	476	gain	
NAAR047-E5-01C08485	1	12	27,470,200	27,495,700	25,500	3	gain	
NAAR028-D6-3139.003	1	12	36,491,900	37,417,300	925,400	12	gain	
NAAR001-A9-8002-202	7	12	36,506,000	37,162,800	656,800	10	loss	
NAAR004-B12-8080-201	2	12	36,506,000	36,697,300	191,300	7	loss	
NAAR020-F12-HI1566	3	12	36,694,800	36,697,300	2,500	3	loss	
NAAR052-F6-HI0682	3	12	44,378,800	130,547,000	86,168,200	321	gain	
NAAR028-C3-3133.003	1	12	128,620,000	128,999,000	379,000	4	gain	
NAAR054-F3-HI0298	1	13	47,048,100	47,569,100	521,000	8	gain	
NAAR054-F4-HI0299	1	13	47,048,100	47,569,100	521,000	8	gain	
NAAR031-G7-3212.003	1	13	63,529,600	65,319,400	1,789,800	9	gain	
NAAR044-C5-01C06331	1	13	65,120,700	65,951,300	830,600	5	gain	
NAAR002-B3-8026-204	2	15	21,490,300	22,083,700	593,400	9	gain	
NAAR015-C12-F-016-003	1	15	21,885,600	22,083,700	198,100	6	gain	
NAAR052-E6-HI0308	1	15	23,325,300	24,495,700	1,170,400	4	gain	
NAAR078-A3-200305415	9	15	49,345,700	100,170,000	50,824,300	190	gain	
NAAR007-C5-8168-202	1	15	57,930,400	58,146,000	215,600	4	gain	
NAAR055-A4-HI0442	2	15	74,290,400	100,170,000	25,879,600	104	gain	
NAAR075-E1-04C36221	2	16	7,668,760	8,435,410	766,650	8	gain	
NAAR029-C8-3169.004	1	16	8,241,130	8,435,410	194,280	5	gain	
NAAR045-A5-01C06730	3	16	56,228,100	56,409,200	181,100	6	gain	
NAAR026-C4-3099.007	1	16	60,141,700	61,581,600	1,439,900	7	loss	
NAAR026-D4-3099.008	1	16	60,141,700	61,581,600	1,439,900	7	loss	
NAAR045-A5-01C06730	3	17	14,691,500	15,108,700	417,200	4	gain	
NAAR022-A10-3023.004	1	18	10,741,600	11,601,400	859,800	7	gain	
NAAR022-H9-3023.003	1	18	10,741,600	11,601,400	859,800	7	gain	

De novo CNVs								
Sample ID	CNV/sample	Chr	Start	Stop	Size	#SNPs/segment	CNV	
NAAR061-A5-HI0128	1	7	121543000	122291000	748000	4	loss	
NAAR054-F3-HI0298	1	13	47048100	47569100	521000	8	gain	
NAAR054-F4-HI0299	1	13	47048100	47569100	521000	8	gain	
NAAR067-A8-HI2741	1	8	3909530	3909710	180	2	gain	
NAAR068-B12-HI1404	1	17	14304400	15237700	93300	10	gain	
NAAR022-H7-3019.003	1	9	70619600	70908800	289200	7	loss	
NAAR026-C4-3099.007	1	16	60141700	61581600	1439900	7	loss	
NAAR026-D4-3099.008	1	16	60141700	61581600	1439900	7	loss	
NAAR027-C6-3120.003	1	4	189303000	189310000	7000	3	loss	
NAAR027-D6-3120.004	1	4	189303000	189310000	7000	3	loss	

**Mapping autism risk loci using genetic linkage and chromosomal rearrangements** (The Autism Genome Project (AGP) Consortium)

**Supplementary Table 4. List of Validated CNVs.**











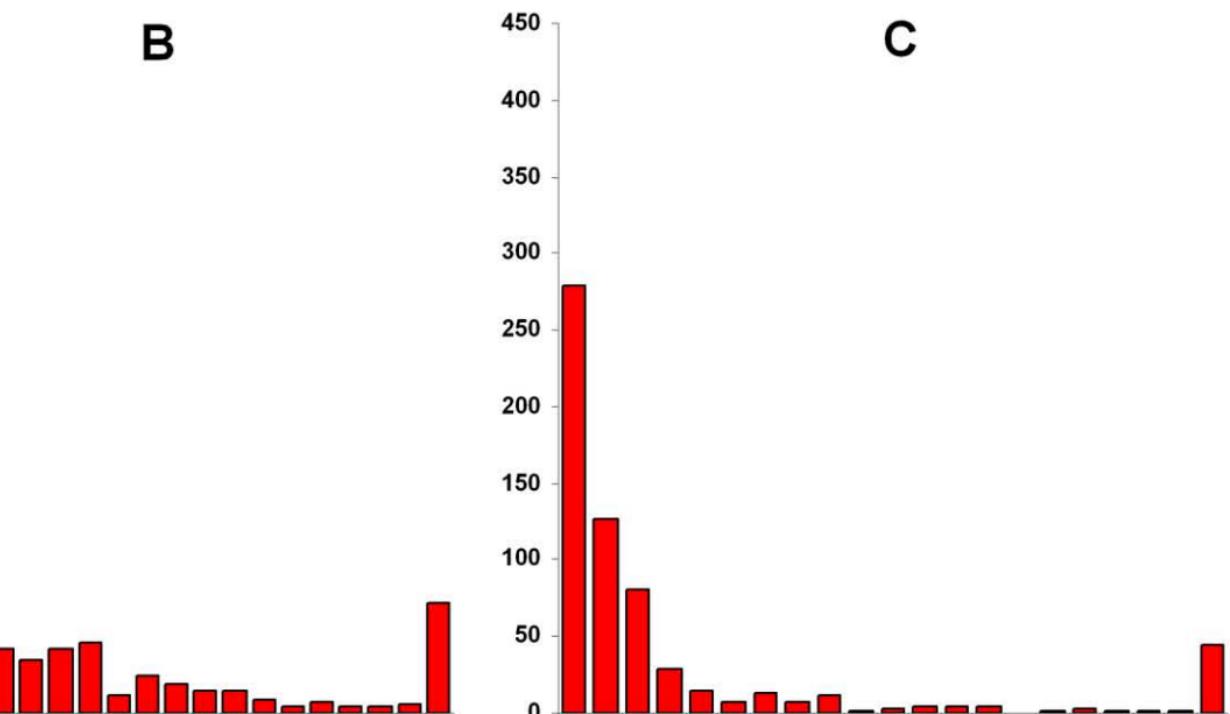
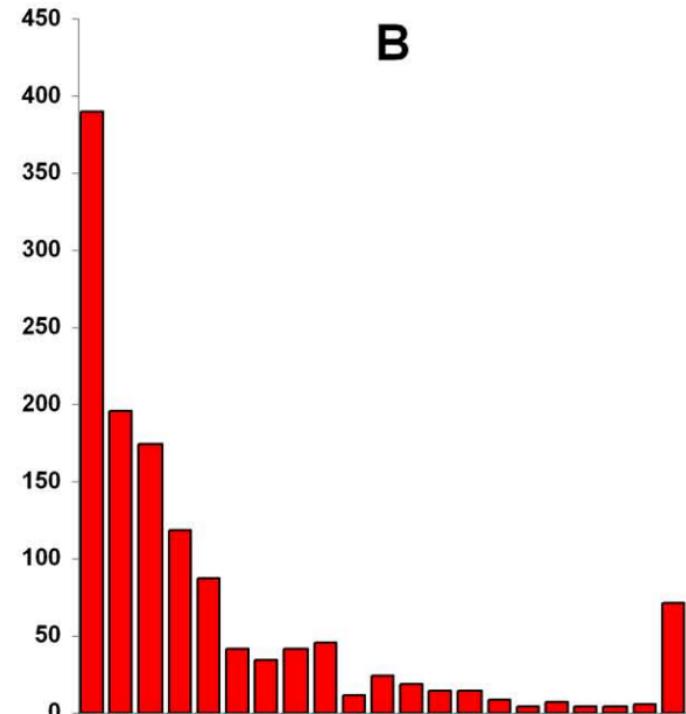
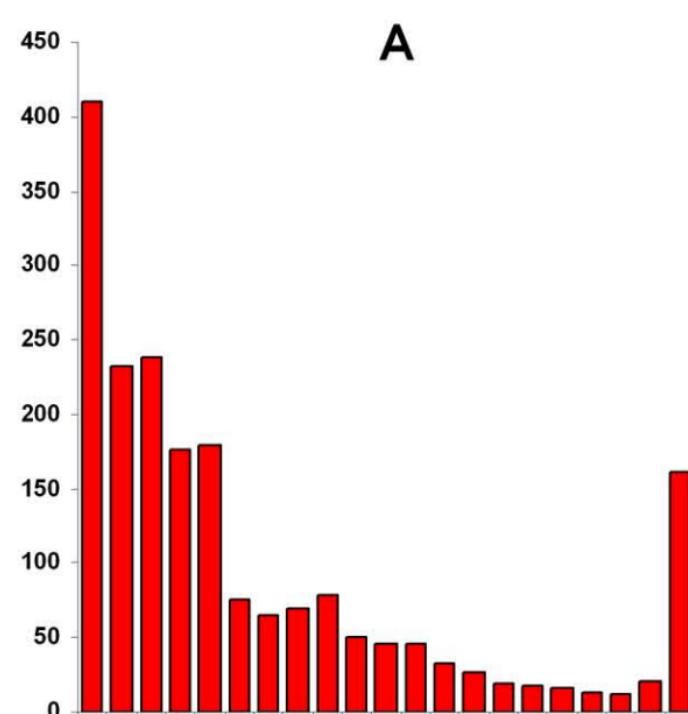


SCAN ID	Family ID	Invd ID	chr	cytoband	start	stop	size	cnv (loss/gain)	Validation
NAAR054-F4-HI0299		1154	4	13 13q14.2	47,048,100	47,569,100	521,000	gain	Familial
NAAR031-G7-3214.003		3212	3	13q21.31\11q21	63,520,000	65,916,400	1,396,400	gain	Familial
NAAR031-A8-3212.005		3212	5	13 13q21.32	64,789,700	65,319,400	520,700	gain	Familial
NAAR044-C5-01C06329		7084	2	13 13q21.32	65,120,700	65,951,300	830,600	gain	Familial
NAAR024-C5-01C06331		7084	4	13 13q21.32	65,120,700	65,951,300	830,600	gain	Familial
NAAR024-B7-3064.003		3064	3	15q11.2\15q12	21,490,300	25,698,400	4,208,100	gain	Familial, Affy Nsp 250K
NAAR024-C7-3064.004		3064	4	15q11.2\15q12	21,490,300	25,698,400	4,208,100	gain	Familial, Affy Nsp 250K
NAAR065-E6-HI0302		1097	3	15q11.2\15q12	21,490,300	25,698,400	4,208,100	gain	Familial, FISH, MLPA
NAAR065-E7-HI0304		1097	4	15q11.2\15q12	21,490,300	25,698,400	4,208,100	gain	Familial, FISH, MLPA
NAAR024-A7-3064.002		3064	2	15q11.2\15q12	21,885,600	25,698,400	3,812,800	gain	Familial
NAAR046-F11-01C08067		7070\8044	6\1201	15q11.2	21,885,600	22,083,700	198,100	loss	Familial, Mendelian Error
NAAR078-A3-200305415		4075	100	15q22.1\15q22.:	49,345,700	100,170,000	50,824,300	gain	Familial, Mendelian Error
NAAR029-C8-3169.004		3169	4	16p13.2	8,241,130	8,435,410	194,280	gain	Familial
NAAR026-B4-3099.006		3099	6	16q21	60,141,700	61,581,600	1,439,900	loss	Familial, Mendelian Error
NAAR026-C4-3099.007		3099	7	16q21	60,141,700	61,581,600	1,439,900	loss	Familial, Mendelian Error
NAAR026-D4-3099.008		3099	8	16q21	60,141,700	61,581,600	1,439,900	loss	Familial, Mendelian Error
NAAR001-D12-8012-111		8012	111	17 17p12	14,304,400	15,237,700	933,300	loss	Familial
NAAR028-B4-3135.002		10581\8135	112	17 17p12	14,304,400	15,237,700	933,300	loss	Familial
NAAR028-C4-3135.003		10581\8135	413	17 17p12	14,304,400	15,237,700	933,300	loss	Familial, Mendelian Error
NAAR028-D4-3135.004		3135\1058	415	17 17p12	14,304,400	15,237,700	933,300	loss	Familial, Mendelian Error
NAAR028-B11-HI1465		1263	4	17 17p12	14,304,400	15,237,700	933,300	gain	Familial
NAAR028-B11-HI1465		1263	5	17 17p12	14,304,400	15,237,700	933,300	gain	Familial
NAAR001-E1-8012-201		8012	201	17 17p12	14,432,900	15,307,700	804,800	loss	Familial, Mendelian Error
NAAR003-A5-8047-202		8047	202	17 17p12\11q17q25.:	33,246,900	76,399,500	43,152,600	gain	Familial
NAAR076-D4-04C36911		5106	3	18p11.132	1,749,000	1,807,190	59,190	loss	Affy Nsp 250K
NAAR067-D10-HI2765		1384	202	18p11.132	1,564,270	1,807,190	242,920	gain	Familial
NAAR067-D12-HI2767		1384	301	18p11.132	1,564,270	1,964,410	400,040	gain	Familial
NAAR022-A10-3023.004		3023	4	18p11.21\18p11	10,741,600	11,601,400	859,800	gain	Familial
NAAR022-G9-3023.002		3023	2	18p11.21\18p11	10,741,600	11,601,400	859,800	gain	Familial
NAAR022-H9-3023.003		3023	3	18p11.21\18p11	10,741,600	11,601,400	859,800	gain	Familial
NAAR031-A8-3212.005		3212	5	18q12.2	32,374,000	32,510,700	136,700	loss	Familial, Mendelian Error
NAAR031-E7-3212.001		3212	1	18q12.2	32,374,000	32,510,700	136,700	loss	Familial
NAAR027-G6-3121.002		3121	2	18q12.2\18q12.:	34,993,000	35,619,700	626,700	loss	Familial
NAAR036-B11-1014-B11-P2		3121	4	18q12.2\18q12.:	34,993,000	35,619,700	626,700	loss	Familial, Mendelian Error
NAAR030-C12-3198.001		3198	1	19q13.3\19p13.:	3,542,590	15,912,900	12,370,310	gain	Familial
NAAR030-D12-3198.002		3198	2	19q13.3\19p13.:	3,542,590	16,332,900	12,790,310	gain	Familial
NAAR041-G10-01C05471		7008	2	20 20p13	95,685	1,358,480	1,262,795	gain	Familial
NAAR041-G7-01C05468		7008	4	20 20p13	95,685	691,220	595,535	gain	Familial
NAAR017-C1-HI2201		1318	2	21 21q22.11	30,538,900	30,983,100	444,200	gain	Familial
NAAR017-C2-HI2202		1318	3	21 21q22.11	30,538,900	30,983,100	444,200	gain	Familial
NAAR063-B1-HI1183_2		1004	4	22 22q11.21	17,506,900	20,306,800	2,799,900	gain	Familial, FISH
NAAR063-A10-HI1180		1004	2	22 22q11.21	18,008,700	19,774,000	1,765,300	gain	Familial, FISH
NAAR053-F1-03C15328		2072	2	22 22q13.33	48,004,600	48,881,300	876,700	loss	Familial, Mendelian Error, Affy Nsp 250K
NAAR072-F11-200501053		2072	1	22 22q13.33	48,004,600	48,881,300	876,700	loss	Familial, Affy Nsp 250K

**Mapping autism risk loci using genetic linkage and chromosomal rearrangements** (The Autism Genome Project (AGP) Consortium)

**Supplementary Figure 1. Binned size distribution of CNVs in batch (A), plate (B) and filtered (C) analyses.**

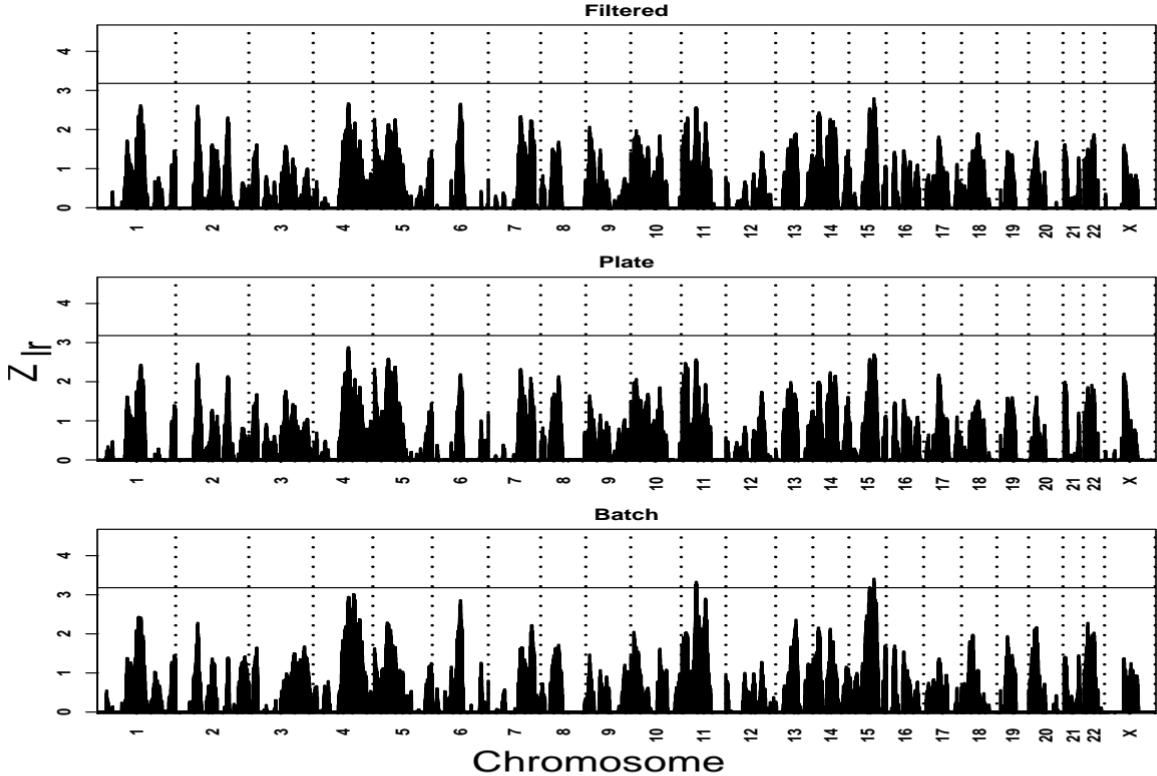
#CNVs



BIN (Mb)

**Mapping autism risk loci using genetic linkage and chromosomal rearrangements** (The Autism Genome Project (AGP) Consortium)

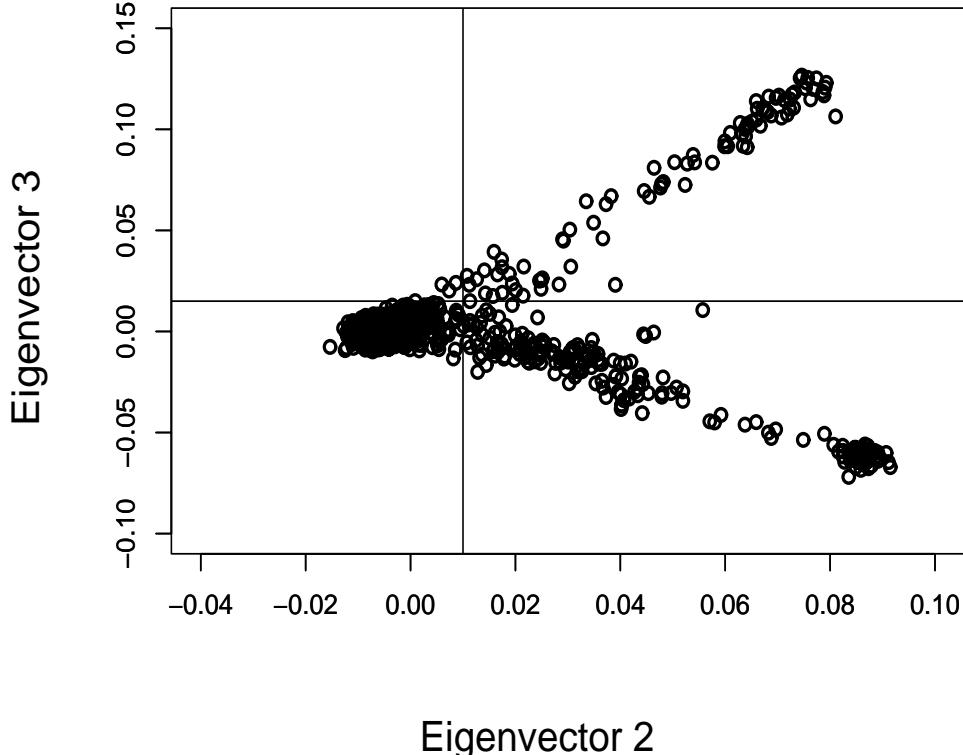
**Supplementary Figure 2. Linkage results due to removing families in which affected individuals putatively carry CNV.**



Supplementary Figure 2. Linkage results due to removing families in which affected individuals putatively carry CNV. Families all fall in the broad diagnostic category. For 11p, the maximum occurs in 11p13 ( $Z_{lr} = 3.33$  at rs2421826). For chromosome 15, there are two up-crossings: the smaller peak occurs at 15q23 ( $Z_{lr} = 3.19$  at rs1372828) and the larger peak in 15q25.3 ( $Z_{lr} = 3.41$  near rs1433452).

**Mapping autism risk loci using genetic linkage and chromosomal rearrangements** (The Autism Genome Project (AGP) Consortium)

**Supplementary Figure 3. Principal component plot used to infer ancestry.**

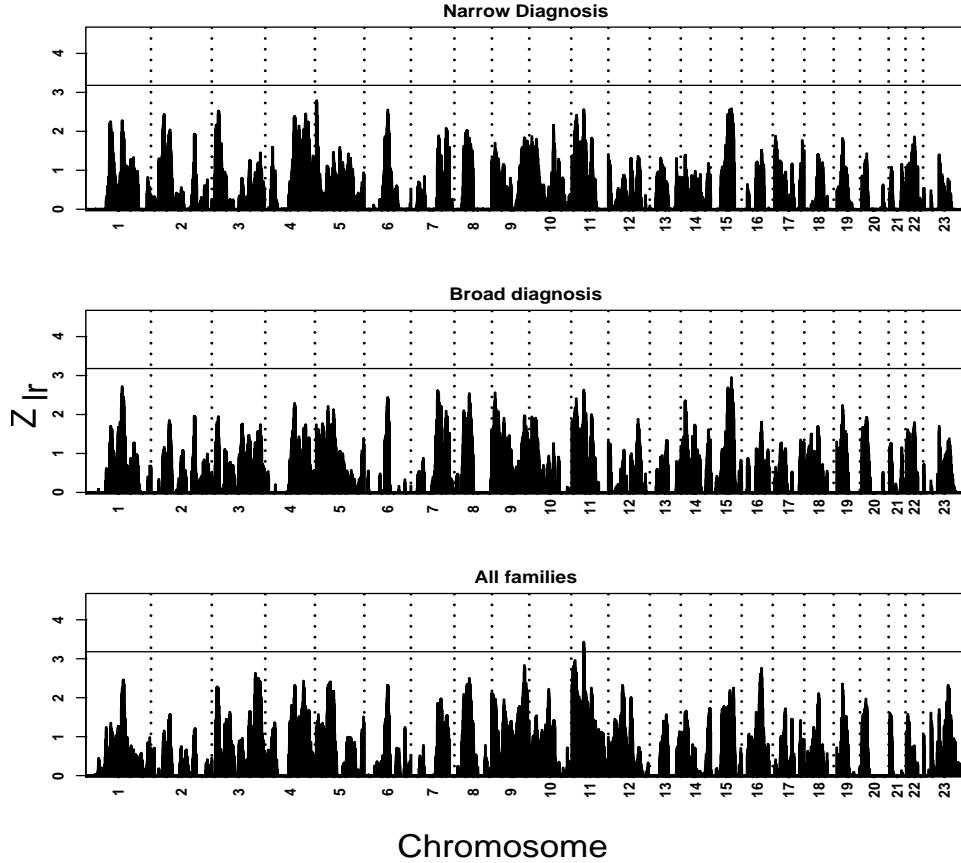


Eigenvector 2

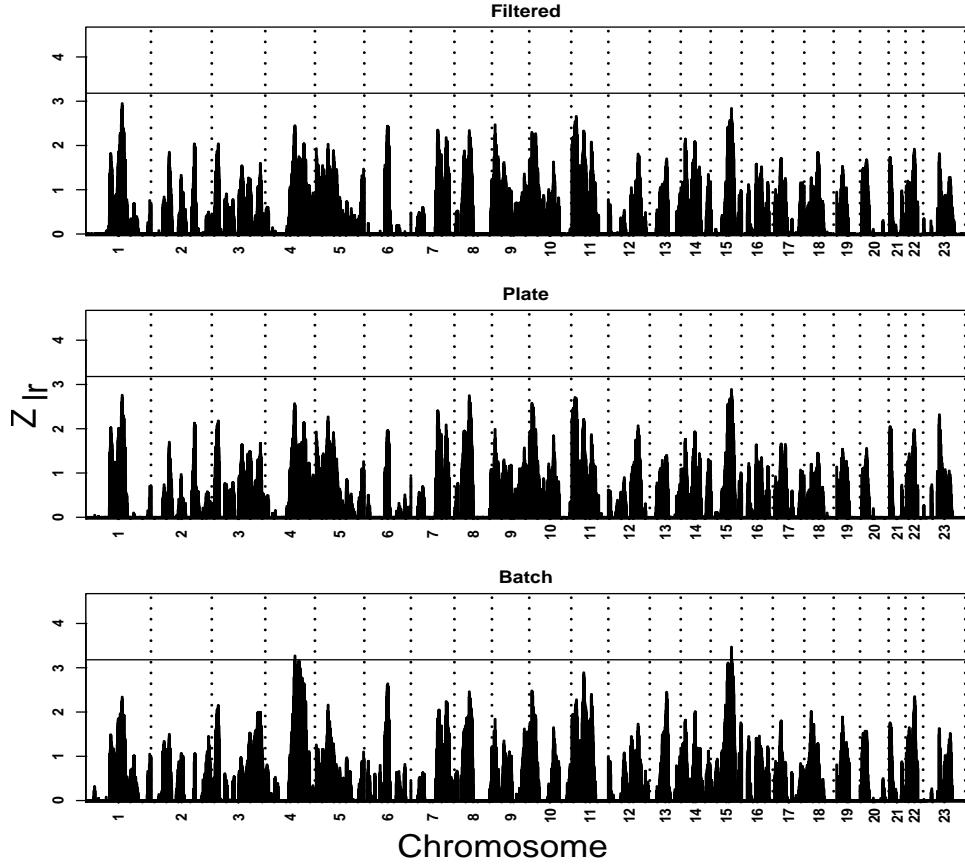
Supplementary Figure 3. Principal component plot used to infer ancestry. A simple way of inferring multidimensional ancestry for  $N$  founders of the pedigrees is to construct an  $N$  by  $N$  matrix  $\Pi$  of pairwise correlations of individuals  $i$  and  $j$  genotypes for all  $L$  loci. For each individual, each locus is coded as 0, 1, or 2 for the number of minor alleles carried. Then principle components can be extracted from  $\Pi$  that represent continuous, multidimensional estimates of ancestry for the sample (Price et al. 2006). Because correlated SNPs can affect the outcome in some settings (BD, unpublished data), we used independent or tag SNPs. Here we plot the second and third eigenvectors ( $E_2, E_3$ ) against one another. The cluster in the lower left quadrant corresponds, when we have information, to European ancestry. We apply a rule that a family is of European ancestry if all founders fall in this quadrant, 995/1168 or 85.2% of families fall in this group. Inferred ancestry was used for linkage analysis, including computing European-specific allele frequencies used for linkage analysis, for testing HW, and for relationship evaluation. Very similar clustering for European ancestry obtains from dimensions ( $E_1, E_2$ ) or ( $E_1, E_3$ ) (results not shown).

**Mapping autism risk loci using genetic linkage and chromosomal rearrangements** (The Autism Genome Project (AGP) Consortium)

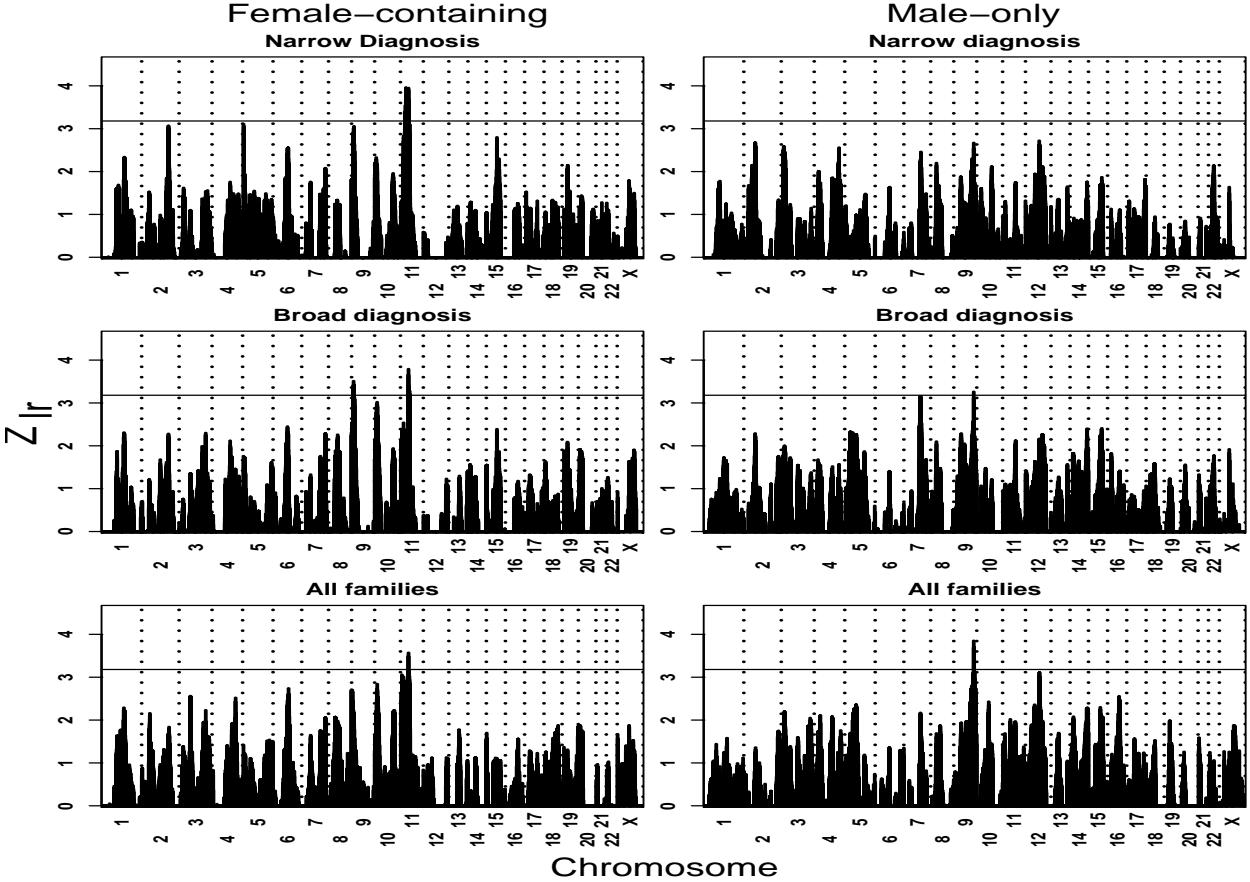
**Supplementary Figure 4. Linkage results obtained by analyzing families inferred to be of homogeneous European ancestry (see Supplementary Figure 3 for methods.)**



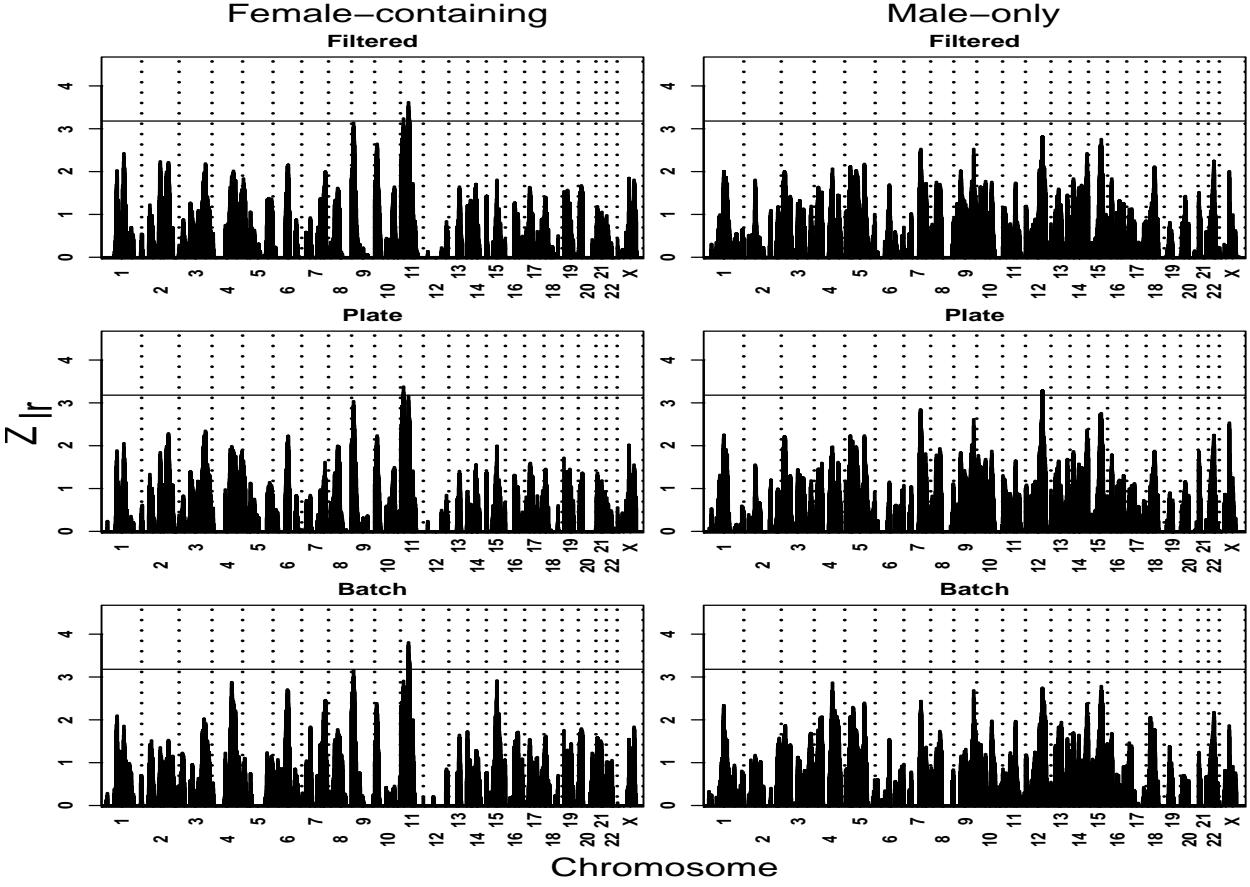
Supplementary Figure 4A. Linkage across the genome for all families of inferred European ancestry, based on levels of diagnostic certainty. Vertical reference lines separate chromosomes, which are ordered. The horizontal reference bar is given at a  $Z_{lr}$  of 3.18, the threshold for suggestive linkage according to the Lander/Kruglyak criterion. The suggestive threshold is expected to be crossed, by chance, once per genome scan. It is crossed once, within 11p12 ( $Z_{lr} = 3.43$  at rs2421826).



Supplementary Figure 4B. For families inferred European ancestry, the effect on linkage of removing families in which affected individuals putatively carry CNV. For the batch method of calling CNVs, the suggestive linkage threshold is crossed twice, within 4q31.22 ( $Z_{lr} = 3.19$  at rs720484; m-p = 0.00006) and within 15q25.3 ( $Z_{lr} = 3.47$  at rs1433452; m-p = 0.002).



Supplementary Figure 4C. Linkage peaks by MO/FC for all families of inferred European ancestry, based on levels of diagnostic certainty. Linkage peaks by MO/FC for all families of inferred European ancestry, based on levels of diagnostic certainty. For FC families and narrow diagnosis, the linkage trace in 11p is complex, crossing the suggestive threshold twice. The first maximum is in 11p14.3 ( $Z_{lr} = 3.96$  at rs726859;  $m-p = 0.002$ ) and the other is in 11p12 ( $Z_{lr}=3.95$  at rs1039205;  $m-p = 0.005$ ). For FC/Broad, the peak falls within 9p24.1 ( $Z_{lr} = 3.51$  at rs1575284;  $m-p = 0.015$ ) and 11p12 ( $Z_{lr} = 3.79$  at rs1039205;  $m-p = 0.009$ ); and for FC/All, to 11p12 ( $Z_{lr} = 3.57$  at rs1039205;  $m-p = 0.046$ ). For all MO families, peak falls within 9q33.3 ( $Z_{lr} = 3.26$ , Broad [ $m-p = 0.002$ ], and  $Z_{lr} = 3.85$  for All [ $m-p = 0.0005$ ], both at rs536861).



Supplementary Figure 4D. The effect on linkage of splitting families of inferred European ancestry into FC and MO families while also removing families in which affected individuals putatively carry CNV. For FC families and filtered subset, two peaks cross the suggestive threshold and maximize in two regions on chromosome 11, within 11p15.3 ( $Z_{lr}=3.24$  at rs871704;  $m-p=0.335$ ) and 11p12 ( $Z_{lr}=3.62$  at rs1039205;  $m-p=0.291$ ); for FC/Plate, to 11p15.3 ( $Z_{lr}=3.38$  at rs871704;  $m-p=0.214$ ); and for FC/Batch, to 11p12 ( $Z_{lr}=3.81$  at rs1039205;  $m-p=0.017$ ). For MO families and plate subset, a single peak crosses the suggestive threshold and maximizes within 12q23.1 ( $Z_{lr}=3.29$  at rs1560020;  $m-p=0.027$ ).