Supplemental Information

Subject Recruitment

Information about patients recruited through the AC was collected on a brief case report form that included demographic and medical-history information for each child participant, including specific ASD diagnosis (autism, PDD-NOS, Asperger syndrome, Rett disorder, or childhood disintegrative disorder) and secondary diagnoses (MR, developmental delay, seizures, and dysmorphic features). Genetic test results were provided to each family by a physician or genetic counselor, and follow-up referrals for evaluations, clinical care, or parental testing were made as appropriate, in accordance with the current practice of each clinic. If a child participant was identified with a genetic abnormality and parental testing was recommended, the parent provided written consent for participation. Results of the genetic testing were obtained from the participant's medical record.

Deidentified genetic test results and demographic and medical-history information from the case report form were entered into a password-protected secure database: the AC Clinical Genetics Registry. The registry was approved by the Massachusetts General Hospital institutional review board and housed on a server at Massachusetts General Hospital. Access to the registry by participating hospitals was provided through a password-protected Web-based application.

Agilent Chromosomal Microarray Methods

The Agilent oligonucleotide array comparative genomic hybridization (CGH) platform was evaluated previously at the DNA diagnostic laboratory at Children's Hospital Boston.[1] The array CGH was performed according to the manufacturer's oligonucleotide array-based CGH for genomic DNA analysis protocol version 3 (Agilent Technologies, Palo Alto, CA). Briefly, 3 μg of DNA (both test and control samples) were double-digested with AluI and RsaI and subsequently purified with QIAprep Spin Miniprep kit (Qiagen GmbH, Hilden, Germany). Digested samples were labeled with Cy3-dUTP or Cy5-dUTP (Amersham Bioscience, Little Chalfont, United Kingdom) by using the Bioprime array CGH DNA-labeling system (Invitrogen Life Technologies, Carlsbad, CA); paired samples were mixed and subsequently purified by MicroCon YM-30 (Millipore, Billerica, MA). Labeled probes were mixed with Cot-1 DNA (Invitrogen Life Technologies), blocking solution and hybridization solution (Agilent Technologies), and hybridized a 244|000 human oligo chip (G244B [Agilent Technologies]). Hybridizations were performed in a 65°C oven on a rotating rack for 40 hours. Arrays were washed with wash 1 and 2 solutions (Agilent Technologies) and scanned immediately by using the Agilent scanner. Data were analyzed by using CGH Analytics or DNA Analytics software (Agilent Technologies).

Affymetrix 500K Assay Methods

Blood samples were received and processed at the Center for Human Genetics, Boston University School of Medicine. Genomic DNA was extracted by using the Autopure automated DNA extractor (Gentra Systems, Minneapolis, MN) according to manufacturer instructions.

Briefly, the 500K assay (Affymetrix, Santa Clara, CA) is two 250K arrays consisting of an NspI (New England BioLabs, Beverly, MA) digest and an StyI (New England BioLabs) digest. Genomic DNA (50 ng/μL) is digested for the restriction enzymes separately. Each restriction digest is then ligated with enzyme-specific adaptors. Using the adaptors as universal sequences, the samples are subjected to polymerase chain reaction to amplify the restriction fragments and generate products between 200 bp and 2 kb. The polymerase-chain-reaction products are purified and fragmented to give products in the 20- to 200-bp size range. The products are then labeled with a labeling reagent and hybridized overnight separately onto a 250K NspI array and a 250K StyI array. The arrays are then stained with streptavidin, and the signal is amplified with a biotinylated antibody. The arrays are then placed into the GeneChip scanner (Affymetrix), where each of the 250K spots on the array is interrogated.

Affymetrix 500K Data Analysis

Copy-number analysis is performed by using the Affymetrix GeneChip Genotyping Analysis software. The arrays are first analyzed in a batch analysis program to determine the genotype call rate, then analyzed with Bayesian RLMM (BRLMM). Once this is finished, the arrays are analyzed with CNAT4 (Copy Number Analysis Tool) Batch Analysis for copy number. This program combines the two 250K arrays into a single virtual chip that can be viewed for copy number. The arrays are compared against a reference set of 25 previously defined normal Hapmap samples. The single-nucleotide polymorphism (SNP) results are then displayed across the chromosomes. Changes in copy number are readily visible on the display. Amplifications/deletions greater than 100 kb are reported. By using the UCSC Genome Browser (Santa Clara, CA) assembly,

any genes in these regions that have copy-number changes are reported.

Affymetrix 5.0 Assay Methods

The SNP Array 5.0 is a single microarray featuring all SNPs from the original 2-chip mapping 500K array set, as well as 420|000 additional nonpolymorphic probes that can measure other genetic differences, such as copy-number variation. This assay now combines the NspI and StyI fractions previously assayed on 2 separate arrays. The steps are the same as for the 500K assay.

Affymetrix 5.0 Data Analysis

Copy-number analysis is performed by using the copy-number feature of Partek Genomic Suite software (St Louis, MO). The arrays are analyzed to determine the genotype call rate. Once this is finished the arrays are analyzed with the copy-number feature. The arrays are compared against a reference set of 25 previously defined normal Hapmap samples. The SNP results are then displayed across the chromosomes. Changes in copy number are readily visible on the display. Amplifications/deletions greater than 100 kb are reported. By using the UCSC Genome Browser assembly, any genes in these regions that have copy-number changes are reported.

Clinical Interpretation of Chromosomal Microarray Data

Identification of novel variants is common in CMA testing, and more common with whole genome arrays. Dozens of CNVs are present in every human genome,[2–4] and the clinical significance of many CNVs is poorly understood. Information about CNV locations and clinical correlations is cataloged in several public databases, such as the Database of Genomic Variants (http://projects.tcag.ca/variation) and DECIPHER (Database of Chromosomal Imbalance and Phenotype in Humans Using Ensembl Resources) (www.sanger.ac.uk/PostGenomics/decipher), which incorporates a suite of tools designed to aid the interpretation of submicroscopic chromosomal imbalance, inversions, and translocations, as reviewed elsewhere.[5,6]

CNV interpretation has been addressed in published guidelines.[7,8] A common approach to the interpretation of VUS involves offering similar testing for the parents to determine if the variant is new or de novo. The presence of similar variation in a parent may lead to a conclusion that identified variants are benign or pathogenic depending on the presence of similar clinical symptoms in a parent. Other clues to pathogenicity include the gene content of genomic variants. Variants including known disease genes are more likely to explain a clinical phenotype. Even if a variant contains a known gene, the type of CNV may affect pathogenicity. Deletions are generally considered more pathogenic than duplication, although this is not a universal rule.

The size of genomic variants also influences pathogenicity, although many relatively large CNVs variants (>500 kb) are familial, and many relatively small CNVs (<500 kb) are pathogenic. A majority of CNVs detected on high-resolution oligonucleotide platforms are less than 150 kb,[4,9,10] and detection of these CNVs complicates clinical interpretation. Overall, each of these factors must be considered before rendering a clinical interpretation of genomic CNVs, as reviewed in greater detail elsewhere.

REFERENCES

1. Shen Y, Irons M, Miller DT, et al. Development of a focused oligonucleotide-array comparative genomic hybridization chip for clinical diagnosis of genomic imbalance. Clin Chem. 2007;53(12):2051–2059
2. Iafrate AJ, Feuk L, Rivera MN, et al. Detection of large-scale variation in the human genome. Nat Genet. 2004;36(9):949–951
3. Eichler EE. Widening the spectrum of human genetic variation. Nat Genet. 2006;38(1):9–11
4. Itsara A, Cooper GM, Baker C, et al. Population analysis of large copy number variants and hotspots of human genetic disease. Am J Hum Genet. 2009;84(2):148–161
5. Van Vooren S, Coessens B, De Moor B, Moreau Y, Vermeesch JR. Array comparative genomic hybridization and computational genome annotation in constitutional cytogenetics: suggesting candidate genes for novel submicroscopic chromosomal imbalance syndromes. Genet Med. 2007;9(9):642–649
6. Firth HV, Richards SM, Bevan AP, et al. DECIPHER: Database of Chromosomal Imbalance and Phenotype in Humans Using Ensembl Resources. Am J Hum Genet. 2009;84(4):524–533
7. Manning M, Hudgins L. Use of array-based technology in the practice of medical genetics. Genet Med. 2007;9(9):650–653
8. Shaffer LG, Beaudet AL, Brothman AR, et al. Microarray analysis for constitutional cytogenetic abnormalities. Genet Med. 2007;9(9):654–662
9. Redon R, Ishikawa S, Fitch KR, et al. Global variation in copy number in the human genome. Nature. 2006;444(7118):444–454
10. Komura D, Shen F, Ishikawa S, et al. Genome-wide detection of human copy number variations using high-density DNA oligonucleotide arrays. Genome Res. 2006;16(12):1575–1584
11. Lee C, Iafrate AJ, Brothman AR. Copy number variations and clinical cytogenetic diagnosis of constitutional disorders. Nat Genet. 2007;39(7 suppl):S48–S54

SUPPLEMENTAL TABLE 1 Variants of Unknown Significance

Chromosome Locus	Type of Change	Size, kb	Coordinates (hg18)
1p13.1	Duplication	1148	115929481–117077952
1p31.1	Duplication	98	70545751–70643192
1p31.3	Duplication	80	65627570–65707722
1p32.1	Deletion	43	59818945–59861885
1p34.1	Duplication	277	45938177–46214819
1p35.3	Duplication	59	28071072–28130320
1q21.2	Duplication	30	149369522–149399354
1q21.3	Deletion	26	150643431–150669253
1q22	Duplication	105	152335528–152441362
1q23.2	Duplication	30	158378189–158408096
1q23.2	Deletion	69	158296040–158365328
1q23.3	Duplication	67	158305161–158372610
1q31.3	Deletion	77	193480150–193556851
1q32.1	Duplication	36	201519752–201556008
1q41	Deletion	174	214006564–214180878
1q43	Duplication	172	234677569–234849353
2p16.3	Deletion	48	48642925–48690613
2p21	Duplication	561	45263776–45824967
2p21	Deletion	111	45142805–45253772
2p23.3	Duplication	222	25010389–25232114
2p23.3	Deletion	123	26526964–26650410
2p25.1	Duplication	43	10443953–10486678
2q12.3	Duplication	192	107182927–107374708
2q14.2	Duplication	128	119883078–120010945
2q34	Duplication	2418	209120272–211538263
3p25.2	Duplication	142	11725108–11866966
3p26.3	Duplication	821	35000–856000
3p26.3	Duplication	487	2184248–2671032
3q21.3	Deletion	22	127738922–127760706
3q21.3	Deletion	22	127738922–127760706
3q26.2	Duplication	101	169267735–169368109
4p13	Duplication	319	43639658–43958804
4p16.1	Duplication	542	9532281–10074307
4q21.23	Duplication	225	87059036–87284649
4q25	Deletion	81	114039979–114120494
4q28.1	Duplication	526	123921769–124447711
4q28.2	Duplication	79	129163803–129242884
4q31.23	Duplication	131	149579044–149709797
4q35	Duplication	331	185959445–186290124
4q35.2	Duplication	711	190538660–191250145
5q31.2	Duplication	703	137463806–138167611
6p22.1	Duplication	230	28525866–28756292
6p22.1	Deletion	51	28979234–29030730
6q11.1	Duplication	833	63255005–64087608
6q16.1	Deletion	959	92350077–93309199
6q21	Duplication	482	106613439–107095209
6q25.1	Deletion	30	151672213–151702033
7p14.1	Duplication	235	39800516–40035332
7p14.3	Duplication	54	33097553–33152539
7p14.3	Duplication	55	33097553–33152539
7p14.3	Duplication	54	33097553–33152539
7p14.3	Duplication	55	33097553–33152539
7p14.3	Duplication	55	33097553–33152539
7q11.23	Duplication	181	75401774–75583095
7q22.1	Duplication	448	99010883–99458579
7q22.3	Deletion	83	106717466–106800374
7q31.1	Deletion	172	109954612–110126676
7q33	Deletion	256	133060000–133316000
7q34	Duplication	118	140256549–140374477
7q36.1	Deletion	52	151379435–151431158
8p11.23	Deletion	59	39128088–39187859
8p12	Duplication	101	38180851–38281364

SUPPLEMENTAL TABLE 1 Continued

Chromosome Locus	Type of Change	Size, kb	Coordinates (hg18)
8p12	Deletion	446	32765436–33211412
8p22	Deletion	45	13082460–13127459
8q13.2	Duplication	180	68092487–68272431
8q21.11	Deletion	266	75519142–75784892
8q21.2	Duplication	202	86539379–86741780
9p13.2	Deletion	70	37409265–37479345
9p21.3	Duplication	298	20567062–20864718
9p22.1	Deletion	133	19487546–19620612
9q31.1	Duplication	700	102343259–103043117
9q31.1	Deletion	412	103427543–103839936
9q31.3	Duplication	53	113716789–113770103
9q34.11	Duplication	52	129436056–129488906
9q34.2	Duplication	75	135447994–135523489
9q34.2	Duplication	285	136013220–136298049
10p13	Deletion	563	16053444–16616223
10q11.21	Duplication	129	42979015–43108175
10q21.1	Duplication	264	58605000–58869000
10q22.2	Deletion	411	75749022–76160342
10q22.2	Deletion	59	74692636–74751408
10q23.1	Duplication	1243	83661754–84904332
10q23.32	Duplication	226	93685380–93911863
10q23.33	Deletion	105	96967222–97072244
10q23.33	Duplication	1146	95979398–97125811
10q23.33	Deletion	114	96422729–96536271
11q21	Duplication	190	95102950–95293406
11q22.3	Duplication	499	104285169–104784882
11q25	Duplication	172	133984000–134156378
12p11.21	Duplication	50	32679281–32730005
12p11.21	Duplication	50	32679281–32430005
12p11.23	Duplication	482	27197587–27679748
13q12.11	Duplication	26	19317333–19343320
13q12.11	Duplication	371	18494397–18865488
13q21.2	Duplication	1024	59327289–60351436
13q31.1	Duplication	273	86073340–86346046
13q32.1	Duplication	73	94741846–94814964
14q11.2	Deletion	54	22294328–22347838
14q13.2	Duplication	61	34280810–34341968
14q24.2	Duplication	163	72478862–72641861
14q32.2	Deletion	9	98250689–98259258
15q13.3	Duplication	390	30935328–31325430
15q13.3	Duplication	164	30080441–30244833
15q13.3	Duplication	147	30083430–30230370
15q14	Duplication	283	32873843–33156596
15q15.3	Deletion	241	41610457–41851765
15q20.1	Duplication	56	87963677–88019538
15q25	Duplication	38	87936797–87975003
15q25.1	Deletion	47	76841291–76888054
16p13.2	Deletion	83	6883110–6966404
16p13.3	Duplication	467	4226109–4693127
17p13.2	Deletion	109	3882214–3991827
17p13.2–p13.1	Deletion	104	6699298–6803080
17p13.3	Duplication	486	1391616–1877367
17p13.3	Duplication	400	879373–1280058
17q12	Duplication	224	34737303–34961446
18p11.31–p11.23	Duplication	485	7075833–7560888
18p11.32	Deletion	66	170229–236407
18q21.2	Duplication	73	46779898–46853028
18q23	Duplication	419	75568996–75987923
19p12	Deletion	276	21505820–21782094
20p12.1	Duplication	415	13515931–13930996
20p12.3	Duplication	43	8801003–8843935
20p13	Deletion	30	4885202–4915563

SUPPLEMENTAL TABLE 1 Continued

Chromosome Locus	Type of Change	Size, kb	Coordinates (hg18)
20q11.22	Duplication	57	33634683–33691704
20q13.32	Deletion	22	57734633–57757317
21q22.3	Duplication	81	42756544–42837739
21q22.3	Duplication	139	42954140–43093465
22q11.21	Duplication	87	19693064–19779911
22q12.2	Duplication	125	29141060–29266316
22q12.2	Duplication	67	29038245–29104867
22q12.33	Duplication	88	34950270–35039172
22q13.1	Deletion	339	37683612–3801900
22q13.2	Deletion	97	39652724–39749329
Xp11.22	Duplication	1097	51614120–52710691
Xp11.3	Duplication	211	44706657–44917073
Xp22.31	Duplication	1628	6463313–8091810
Xp22.31	Duplication	235	6957788–7192761
Xq12	Deletion	284	65657077–65941741
Xq12	Duplication	186	65657077–65842988
Xq21.31	Deletion	217	87807468–88024116
Xq22.33	Deletion	141	18654–159978
Xq27.3	Deletion	120	144135904–144256200
Yp11.2	Deletion	287	6696721–6984030
Yq11.221	Duplication	166	15380259–15546437

SUPPLEMENTAL TABLE 2 Copy-Number Variants

Chromosome Locus	Type of Change	Size, kb	Coordinates (hg18)
1p31.1	Deletion	284	79993406–80278245
1p33	Duplication	210	47421885–47631217
1p33	Deletion	66	49694563–49760722
1p33	Deletion	66	49694563–49760722
1q31.1	Duplication	438	187929481–188367054
1q31.1	Deletion	102	185910650–186012380
1q42.12	Duplication	96	223316944–223413657
1q42.13	Deletion	100	224712357–224804494
1q44	Duplication	742	246138090–246880909
2p16.2	Duplication	127	54214268–54341696
2p16.3	Duplication	297	51966666–52264129
2p16.3	Deletion	108	51236317–51344921
2p16.3	Deletion	65	50793646–50859380
2p16.3	Deletion	173	52264070–52437533
2p22.3	Duplication	682	32496047–33178943
2p25.3	Deletion	160	74669–234175
2q11	Duplication	68	99221389–99289230
2q13	Deletion	60	110258768–110258827
2q22.1	Deletion	199	140192516–140391809
2q32.3	Deletion	159	194033989–194193963
2q34	Deletion	134	213900382–214035255
2q34	Deletion	134	213900382–214035255
2q37.1	Deletion	72	230893123–230965712
2q37.3	Duplication	81	241348104–241429332
2q37.33	Deletion	171	242505261–242677125
3p24.2	Duplication	128	25839402–25968376
3p24.3	Duplication	269	22525732–22794743
3p25.1	Duplication	97	12546448–12643905
3p25.1	Duplication	149	12625788–12774925
3p26.3	Duplication	570	832141–1402519
3q13.12	Deletion	208	108148394–108356756
3q13.13	Deletion	82	110332728–110414189
3q13.32	Duplication	91	120209074–120300196
3q25.1	Deletion	43	152985594–153029030
4p15.2	Duplication	298	26669685–26967699
4q13.1	Deletion	—	64012685–64196454
4q13.2	Duplication	37	70028556–70066323

SUPPLEMENTAL TABLE 2 Continued

Chromosome Locus	Type of Change	Size, kb	Coordinates (hg18)
4q28.3	Deletion	213	135218818–135431839
4q28.3	Deletion	236	135162686–135399619
4q31.23	Deletion	133	150087315–150220194
4q32.1	Duplication	27	156343823–156371627
4q32.3	Duplication	51	165729958–165780335
4q33	Deletion	82	171846140–171928407
4q35.2	Duplication	355	188707151–189062658
4q35.2	Duplication	589	189674197–190263604
5p14.3	Deletion	94	20822596–20917015
5p15.2	Deletion	47	12739815–12787149
5p15.2	Deletion	48	12739815–12787149
5p15.2	Deletion	421	12481203–12902583
5p15.31	Deletion	155	7266329–7421002
5Q12.1	Duplication	56	59751869–59807133
5q12.1	Duplication	56	59751869–59807133
5q13.2	Deletion	277	152184917–152461926
5q13.2	Duplication	26	71700589–71727409
5q14.2	Duplication	242	81201023–81443539
5q21.1	Deletion	441	97555112–97996776
5q35.2	Duplication	51	177310142–177361603
6p12.1	Duplication	31	57025567–57056653
6p12.1	Duplication	31	57025567–57056653
6p22.2	Deletion	108	23968001–24076225
6p25.1	Deletion	208	4202390–4410302
6q14.1	Duplication	177	81777831–81955185
6q16.3	Duplication	349	100400517–100749562
6q24.1	Deletion	240	140809155–141049958
6q26	Duplication	332	162164490–162496284
6q26	Deletion	537	162822273–163360150
6q27	Duplication	237	168162397–168399768
6q27	Duplication	240	168086690–168324061
6q36.11	Duplication	82	109698258–109780892
7p15.3	Deletion	79	19991112–20070362
7p21.11	Deletion	152	19895481–20047718
7q11.21	Duplication	558	64284236–64833882
7q11.21	Deletion	496	64317152–64813826
7q11.23	Duplication	489	75977218–76461345
7q22.1	Duplication	159	100753847–100913113
7q31.31	Deletion	147	118653907–118801848
7q31.33	Deletion	675	124841815–125517460
7q31.33	Deletion	22	124532475–124555093
7q31.33	Deletion	22	124532475–124555093
7q34	Deletion	64	142535965–142600790
7q35	Duplication	528	143056351–143584405
7q36.3	Deletion	229	158582792–158811327
8p11.1	Duplication	590	43571445–43647122??
8p11.21	Duplication	590	43057445–43647122
8p23.1	Deletion	68	10997906–11066283
8q12.1	Duplication	45	57215366–57260887
8q12.1	Duplication	45	57215366–57260887
8q12.1	Duplication	45	57215366–57260887
8q12.1	Duplication	45	57215366–57260887
8q21.3	Duplication	125	87244329–87369756
8q21.3	Duplication	125	87244329–87369756
8q22.3	Duplication	58	104597386–104655609
8q23.2	Deletion	631	111851857–112483011
8q24.1	Duplication	111	130477937–130589141
9p21.1	Deletion	232	30392242–30624146
9p21.1	Deletion	517	29908743–30425394
9p21.1	Duplication	468	30490204–30958741
9p21.2	Deletion	149	26264518–26413269
9p23	Deletion	376	11971564–12347073
9p23	Duplication	354	10776075–11130940

SUPPLEMENTAL TABLE 2 Continued

Chromosome Locus	Type of Change	Size, kb	Coordinates (hg18)
9p24.3	Deletion	198	1569467–1767542
9p24.3	Deletion	50	194193–244712
9q21.31	Duplication	168	80709888–80877058
9q34.3	Duplication	157	137291390–137449079
10p11.21	Duplication	112	44567691–44679097
10p12.1	Deletion	92	27653437–27745932
10p14	Deletion	125	9761044–9886913
10p15.3	Deletion	106	2429525–2535161
10q11.21	Duplication	112	44567691–44679097
10q11.21	Duplication	124	44567691–44691321
10q11.21	Duplication	124	44567691–44691321
10q11.21	Duplication	112	44567691–44679097
10q21.1	Duplication	467	56165984–56633390
10q21.1	Deletion	65	56296177–56361367
10q21.1	Deletion	65	56296177–56361367
10q25.1	Duplication	800	109978403–110778833
10q25.1	Duplication	192	107099052–107291781
10q27	Duplication	330	133145614–133476839
11p11.12	Duplication	137	51244490–51381967
11p12	Deletion	365	39362743–39727938
11q11	Duplication	148	55225136–55373795
11q11	Deletion	82	55124730–55207364
11q14.1	Deletion	93	81632029–81725288
11q14.2	Duplication	320	86760405–87080566
11q25	Duplication	35	134373558–134409273
11q25	Duplication	472	133761059–134237689
11q25	Duplication	357	133859024–134216882
12p12.3	Duplication	132	19350942–19483375
12q13.13	Duplication	22	49707910–49729183
12q24.12	Duplication	142	110651926–110793312
12q24.12	Duplication	125	110668504–110793312
13q12.11	Duplication	26	19317333–19343320
13q12.2	Duplication	715	22739623–23454108
13q21.1	Deletion	112	54441320–54553418
13q21.2	Duplication	143	58322410–58465138
13q21.31	Duplication	119	61369549–61488488
13q21.32	Deletion	118	65258536–65376868
13q31.3	Duplication	60	89219673–89279955
13q32.1	Duplication	69	96126817–96195296
14q12	Deletion	188	27092217–27280779
14q21.1	Deletion	239	40065729–40304402
14q21.2	Duplication	366	40779816–41145260
14q21.2–q21.3	Duplication	367	42926236–43293623
14q21.2–q21.3	Deletion	1291	42778197–44069699
14q21.3	Deletion	105	47856523–47961395
14q32.33	Duplication	143	103864868–104007328
14q32.33	Duplication	105	103741120–103846676
15q13.3	Duplication	329	29885962–30214161
15q13.3	Duplication	489	29809025–30298155
15q22.2	Deletion	94	61018297–61113122
15q25.2	Duplication	327	83616606–83943605
15q26.3	Duplication	819	98251436–99070776
16p13.2	Duplication	39	8941100–8980711
17p13.2	Deletion	33	5683464–5716760
17p13.3	Duplication	271	746560–1017867
17q12	Duplication	43	31461588–31504608
18p11.31	Duplication	425	4035292–4460508
18q12.3	Duplication	357	36639472–36996954
18q21.1	Deletion	55	44239262–44294629
18q21.2	Deletion	231	49539385–49770946
18q22.1	Deletion	143	63780172–63923394
18q22.1	Duplication	126	60282237–60408993
18q22.1	Duplication	836	63847444–64683523

SUPPLEMENTAL TABLE 2 Continued

Chromosome Locus	Type of Change	Size, kb	Coordinates (hg18)
19p	Deletion	61	6909753–6970105
19q12	Duplication	559	32964337–33405283
19q13.2	Deletion	170	44828229–44998212
19q13.33	Duplication	37	54593738–54630293
19q13.42	Deletion	31	60745205–60776391
19q31.31	Deletion	463	47986294–48449604
20p11.21	Deletion	74	23675418–23749731
20p11.21	Deletion	77	23653059–23730645
20p12.1	Deletion	36	14633390–14669925
21q21.1	Deletion	80	22349931–22429983
21q22.11	Duplication	413	32028581–32441123
21q22.2	Deletion	50	39284183–39334324
22q11.21	Duplication	262	20643128–20904820
22q11.22	Deletion	261	20643128–20904820
22q11.22	Duplication	261	20643128–20904820
22q13.31	Deletion	73	45579947–45653281
22q13.31–q13.33	Deletion	264	45694378–45729440
22q13.33	Deletion	68	48229988–48298677
22q13.33	Deletion	80	48229988–48291943
22q13.33	Deletion	62	48229988–48291943
Xp11.3	Duplication	40	46252456–46292633
Xp11.4	Duplication	192	37699655–37892051
Xp21.1	Duplication	112	33402422–33514518
Xp22.31	Duplication	549	7542546–8091810
Xp22.31	Duplication	125	8226181–8352011
Xp22.31	Duplication	254	7836967–8091810
Xq12	Deletion	35	65572252–65608045
Xq13.3	Deletion	54	74689105–74743044
Xq21.33	Duplication	53	96661202–96714326
Xq22.3	Duplication	61	105811010–105872847
Xq24	Duplication	188	119869413–120057907
Xq25	Deletion	36	124247248–124388478
Xq28	Duplication	16	153980689–153997205
Xq28	Duplication	712	153703704–154415469
Yq11.221	Duplication	19	14679579–14698135