Supp. Methods

PCR Primer Sequences

Case Number (*Gene*)

Case 7 (*FAM58A*)

F5	AGAGCCAGAAGAGAGTACCTAGACCCAGAG
F4	ATAAAGGCCTGAGTGAGAATAGCTGACCATC
F3	GAGAAGAAGTAGAAAGTGCGAAGAGCTGAGT
F2	CTATTGTTTAGTCCCTAGGTCACCTTTGTGC
F1	GAGTAAGTCCAGATTGAGCCAAAGTCCATAC
R2	GAAAGTAACCTATGTATCCCTCCTGCATGGT
R1	CTGCTGCTTTTTGTCTTATAAGCAGATGGACT

Case 8 (*HPRT1*)

F1	TCTAGTACAGACGTCCTTAGAACTGGAACCTG
R1	AGTAGCTAGGAATTTTTGTAGCTCCGCCAAC

Case 11 (*NRXN1*)

Fs	GATGATTCCCGTAGTATCAGCTAATCAGTGG
F1	ACAACCTAGGCCTGATCTAACACTTCTTTCC
F2	GCCTCTGGTTAGGAGAATTAGGAGAGACTG
R2	CTAAGGCATGTTTAGTCTGGAACTGACAACC
R1	CTGCCCTGTTCTGGTATTGTAGCCCTAAAC
Rs	GCTCTGGAAAATCTAGTACTTGGTTGGGTGA

Case 15 (*JAG1*)

F sure 1	CCCGTGGGAACAGTTATTAGGAGAACAGTC
R uncert 1	AGTCCTTTCCTCTATAGTCTGTCGCAACTAGG
R sure 1	TAAAAAGAAACTCTTTGGGCATAGCCAGTGAC

Case 17 (*SLC1A1*)

F uncert 1	GTCAGAGGAATAAACATGAGCTGATAACAGGA
F uncert 2	GCCTGTAAGTACCAGGCAACAGATTCTAGC
F uncert 3	TTTCCCCAAGCTATTTATATCTCCCCCATT
F uncert 4	GAGCCCCACTCCTCAGAAGTAACCACTATT
F uncert 5	CTCTGCAATCCTCTTCTCCTACAAGCTTTC
F uncert 6	GCCCACATCTGGAAGCTGTAAGTAACAAGTA
F uncert 7	AGCTTTTGTTATCGTTTACTACGGACACTGAG
F uncert 8	CTCGGGTAGGTTGAGATGGTCAGTTTATTCT
F uncert 9	CACCCTACTCAGAAGGAGCTTTGGTTACTAAG
F sure 1	GAAGCCTCTCTGATTACCTCACACAAACATC
R uncert 1	GGAGAGGCTCAGAGATTAGGCTCTCTGTAGTT
R uncert 2	CTGGTAACTTATGTGTGGTCAGGACAAACTG
R uncert 3	CTGATTATGAAAGGCAGGAGAAAATCACTGAG
R sure 1	CCATGTGGTTAATAACTAAACGACTTCCTG

Case 17 (*MCCC1*)

F uncert 1	GAGTCACCTATGCTTGGAGTTATTTCTGGTG
F uncert 2	AGCATCCCTTGAAGTAGACCATTTAGAGCAC
F sure 1	CACTGGTGTGAAACTAAAGTGTCTCAGGATAA
R uncert 1	CTTGGTTGTTTAATCATCTCTGACTGTGGTCT
R sure 1	CCCTGTTTAACTTCCGTTTATTTCTCTGGTCT

Case 18 (*CNTNAP2*)

F sure (F3)	TACTGATCTTGCCAGAAGGAAGAAATTAGAGC
R sure (R5)	AGTGGCGTTAGGAGTACAGATATGAGGGAGAC

F uncert 1 (F1)	CAACTGCTGCTCAGTAGTAGGTCTTACACTCC
F uncert 2 (F2)	GGGAGAGCTTAGAATTCCAGAGACCCATAC
R uncert 1 (R1)	ATCAGCACACACTACAACCAAGTAAGCGTCT
R uncert 2 (R2)	TCCACTCTGTAAATTCAAGGCTACTGAGTTTG
R uncert 3 (R3)	CCAGCTCAGTTCTAGGCTCCTAATTAAAGTG
R uncert 4 (R4)	AGGGTAAAGAGATAATGGATGAATGAGGCACT

Case 19 (*ALDOA*)

F sure 1	AATGCTGCTTAGACTACAGGTCAGACATTGAT
R sure 1	GTACTCAAGGGCCAGACTCCTCCTATAACACT
F uncert 1	CTGACATACCACCTAAAATAAACCCAAGATGG
F uncert 2	CCTAACTCAGCCTCTAGCTTCTCCAAACCT
F uncert 3	CTACAATACTTCACACGGTAGCCAGTAGCC
R uncert 1	CAACTTAGTTCTCAGTTCTCAGGGTTGTTGG
R uncert 2	CCCTGGCTATTCACTTCAAATAGACAGAAGG
R uncert 3	GAATTGGGCTGTGCTACTGTCAACAGAACT

Case 21 (*FHIT*)

F uncert 1 (F1)	GATTGGTTTTATAGGCATCAGTGTGGATGT
F uncert 2 (F2)	CTTCAACGCTCATTAAAAGCACAACTCACTAC
F uncert 3 (F3)	CTCTGCCACCAGCCTCAGACTTAGTTCATA
F uncert 4 (F4)	GTACTTGTCACGATGCTGACACACAGAGAG
F uncert 5 (F5)	GTTTAGGAGCAGAGGATCACCCGTACTACTGT
R uncert 1 (R1)	GACGGAGGTTAAGTATTTTGAGGAGAGGTGT
R uncert 4 (R2)	TGTAGCAGTGTCATAGCAAAATTCTACCTGAT

Case 22 (*TEK*)

F sure 1	GGAAGTTACTCAAGATGTGACCAGAGAATGG
R sure 1	AAGTAAGGCTCAGAGCTGATGTTGATGACAG
F uncert 1	CTTTAAGAATACTTGGGATTGGAGAAGGATGG
F uncert 2	GGTAAACTCTGGACAGCAGTGAAACTCTGG
F uncert 3	TAACAATAACAGCATCTCAGGCTGATGAAC
F uncert 4	GATTATTAAGACTTGCTACCACCCCACAAGG
R uncert 1	GCATAGCCTGGGCTTCTTATTAAGTGAGTAAT
R uncert 2	TACAATGCAGAACCTTTCAGATTTCAGAGGAC

Case 23 (*EXT2*)

F uncert 1	CAGAGTATTTACCAGAGGTGGGTAGAGTTCTG
F uncert 2	GGGAAGAGGTGCTACTTACACTTGCTAGAGAC
F uncert 3	GGATGAGACATAAGATACAAGGGCATGCTG
F sure 1	GAAGGTAAGAAGCCTTAGTGCCTCTCTCAG
R uncert 1	GAGTCAAGGGAAGTGGTATTCAAGGAGACAT
R uncert 2	ATGGATCACAGTAAAGTGGAAGGGCATACAG
R uncert 3	AAATATCACCTATGGTCTGGAGATCAAGCAAC
R uncert 4	GAAGAAAACAGGCTTTCCTACATGGTCTAGC
R sure 1	TCAGCCTCAGCTATGTAAGTAAGAACCGAGT

Case 24 (*TTC8*)

F uncert 1	GAATTATAACCAGGACATATGGTGGTCTTGCT
F sure 1	CCTACATTCAACTGCTGATCATATGGGAAA
R uncert 1	GTTAAGAGGCTATGAAGACGATTCCCTCTAC
R uncert 2	CCCAGGTCTATTTTACTACACAGGAACACCT
R uncert 3	AAGTCCAAAAGTAGGAGGAATTTTGGCAGA
R sure 1	GACAGAAACTCAAGTTGCTCATGTTTCCAGAT

Case 25 (*REEP3*)

F uncert 1	GTCTGTGGTACTTCTAATTACTGCAGCCTACC
F uncert 2	GCTCTCTGACGAAGTCCAAACTAGATAGCAT
F uncert 3	ATGGTATGTATTCTGAGCCTTTCTTCCCTAAG
F sure 1	CTGTGGGACAAAGACCATACCAACCTCTAC
R uncert 1	CTTGGCCAATACTCTGAGGAAGTCCTGAAT

R uncert 2	CGTTACCAAGGACAGACCATAAGGAGAGTG
R sure 1	ATTAAGGTGTTTTTCCCCTTCTCAGTCTTC

Case 26 (*MSH6*)

F uncert 1	GCACTTCTATGGTCCAGATGTTAGAGGGTAAG
R sure 1	GTGACAGTGGGTATAAAACAGCCTGAAAGTG
F sure 1	ATCTACCAAGAAGGGCTGTAAACGATACTGG

Case 28 (*KIF7*)

F sure 1	CACAGATCCCTGTCTAGGAAATCGACTCTT
R uncert 1	ATCAGAGGTCTCAGAGGTGAAGACACCAAC
R uncert 2	CTCAGTGGCTATATGGGGCATACTCTTCTC
R uncert 3	CCCACTCTATTAGCTCCCACTCTATTGCAC
R uncert 4	AAATTTGGTATTCTCATGCTTTCCCCTCTAGC
R uncert 5	CCTCTCCTCTAAAGCCCAGCTTAATTCCAG
R uncert 6	ATCTAGAGACCTCTTTGGCCTTGGTTCCTC
R uncert 7	GAGAGAGGCGTAAAATGGTCAAGTACATGGT
R uncert 8	TTCTAAGAAGTGGGAATTCCTCCCTCAACTC
R sure 1	CTCTCCAAGAGAGTATTGCATCTGGAGTTC

Case 29 (*KIF1B*)

F uncert 1	CTGACAGGAGAGCTTACATAGTCTTTCTTTCTTC
F uncert 2	GGGTTCATCAGATGTGACCATGATATAAGAAG
F sure 1	CCTGTCCCATGTGAAGTTTGAATAGATGTAAC
R sure 1	CCATAGACACTTCTCCTCTGACTCCCATAG

Case 30 (*DLG3*)

F uncert 1	AAGATCTATGACAAAGCCATGAAACTGGAG
F sure 1	CTCTGAGAGGGCAGCTTAGCAGATTTTTAG
R uncert 1	AGGGAAGAGGGACTTGATTTCTTCTGTTCAC
R sure 1	CAGAGTCTGTCTTTCCATCAGTCCTCCTCT

Case 31 (*NRXN1*)

F sure 1	GACTTCCCATCTCCCCAGTAACTCTGTATTA
R sure 1	CTGACAGTGCTAAGGGGAACTAGCCTTTGT
F uncert 1	AGCTGTCTTTCTGGTGTACTCTCTCAGGGTAG
F uncert 2	GCTAACACCCTCATCATTAGCACACAGTAG
F uncert 3	GGACTCCTGCCTTTACCTCTGCTTTATGAC
R uncert 1	GTTCCTCTATAATTAAGCATGCCTGGGCTCT
R uncert 2	GCTGTGTTCTAATGTTACCCATGTCTAGCTG

Control Primers

CRTL F sure	CTAGAAGGAACCTAGATAGGTCAAGCCTCTGC
CTRL R sure	AGAGGAGCTTCAGATGCTGGAAAGCTAGAG

Commercially Available MPLA Probe Sets (MRC-Holland)

Case Number (*Gene*): Kit Name

Case 1 (*MECP2*): **P015-D2**
Case 2 (*PTEN*): **P225 PTEN**
Case 3 (*EP300*): **P333-A1 EP300**
Case 5 (*CREBBP*): **P313-A1 CREBBP**
Case 14 (*EYA1*): **P153 EYA1**

Custom MLPA Probes

Case Number (*Gene*)

Case 6 (*ZDHHC9*):

Probe	Ligation Product Length	Left Probe Name	Start (ChrX)	Left Probe Sequence	Right Probe Name	End (ChrX)	Right Probe Sequence
LAT	104	LAT-F		**GGGTTCCCTAAGGGTTGGA**CCTGCTGCTGCCCATCCTGGCCATGTTGATG	LAT--R		GCACTGTGTGTGCACTGCCACAGACTGCCAG**TCTAGATTGGATCTTGCTGGCAC**
ZDHHC9-1	108	ZDHHC9-1-F	128,767,601	GGGTTCCCTAAGGGTTGGACAGAGGTCTCTGTGACTGCCTCTGGACTCAGCA	ZDHHC9-1-R	128,767,666	CGTGCAGCAGCTTGGGAGGATTTGAGCCAGTCTTCTAGATTGGATCTTGCTGGCAC
ZDHHC9-2	112	ZDHHC9-2-F	128,765,371	GGGTTCCCTAAGGGTTGGATCACCACAGCCAATTTCCACCTGCCCCCAGAGGTT	ZDHHC9-2-R	128,765,440	TGGGATCAGTGCCAACCATCCTGGCCTGGGAAAGTTCTAGATTGGATCTTGCTGGCAC
ZDHHC9-3	116	ZDHHC9-3-F	152,946,030	GGGTTCCCTAAGGGTTGGATCTTTGAGGGAGCTGCAGGTGGGGCCCGAATGAAATA	ZDHHC9-3-R	152,946,103	AAGTGACGCTTGAAATGCTGTGTTCCCAACCACGACTTCTAGATTGGATCTTGCTGGCAC
ZDHHC9-4	120	ZDHHC9-4-F	128,772,506	GGGTTCCCTAAGGGTTGGAGTAAATTAGCCTCCGCCCTCTCTATATCGACCCAGCCTT	ZDHHC9-4-R	128,772,583	AAGTCAGGAACACTTACTGGGCTCTGTGGCAAGAGGCTGTCTAGATTGGATCTTGCTGGCAC
ZDHHC9-5	124	ZDHHC9-5-F	128,767,495	GGGTTCCCTAAGGGTTGGAGATTTGTGGGCAATGCTGGCACTTGGTGGCCAGGAGAATCT	ZDHHC9-5-R	128,767,576	TCTGACCCCACTCTCCCTCCTCTTCAGTCCTGAAGACCCCATCTAGATTGGATCTTGCTGGCAC
ZDHHC9-6	128	ZDHHC9-6-F	128,764,757	GGGTTCCCTAAGGGTTGGAGGAGGGGGCTGGGTTGCTAGGTTACTACTAGAGCCAATCCAAG	ZDHHC9-6-R	128,764,842	TGGTCCCAGAGGGGTACCAGATACAGGACAGGTCCTTCTCTCTTCTAGATTGGATCTTGCTGGCAC
ZDHHC9-7	132	ZDHHC9-7-F	128,768,210	GGGTTCCCTAAGGGTTGGATAGACACTGAACTCTTCCTCTCAGCCCCCTGATCACACTGATGCT	ZDHHC9-7-R	128,768,299	ACAGATATGCAGCCACCAACACCAAACTCAGAACCAACACCAAGCTCTAGATTGGATCTTGCTGGCAC

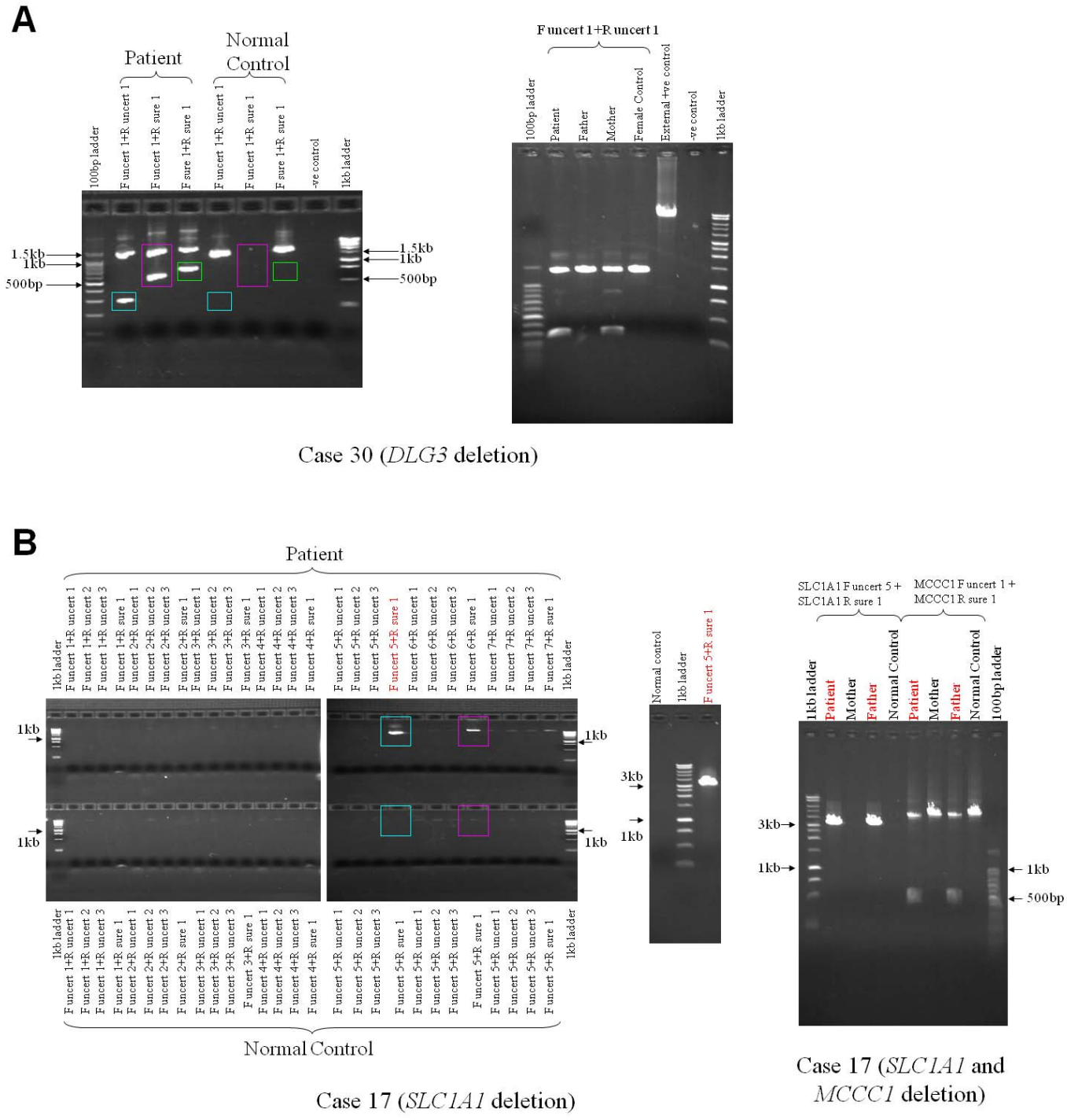
Case 16 (*RFC2*):

Probe	Ligation Product Length	Left Probe Name	Start (Chr7)	Left Probe Sequence	Right Probe Name	End (ChrX)	Right Probe Sequence
LAT	104	LAT-F		**GGGTTCCCTAAGGGTTGGA**CCTGCTGCTGCCCATCCTGGCCATGTTGATG	LAT--R		GCACTGTGTGTGCACTGCCACAGACTGCCAG**TCTAGATTGGATCTTGCTGGCAC**
RFC2-1	108	RFC2-1-F	73,320,250	GGGTTCCCTAAGGGTTGGATCAGCGGGCTGTGAGTGGGGATTGAGGACTTTC	RFC2-1-R	73,320,315	CTACCAGAAACCTGAGTGCCCCAGCATGCCCTTTCTAGATTGGATCTTGCTGGCAC
RFC2-2	112	RFC2-2-F	73,249,921	GGGTTCCCTAAGGGTTGGATCTGGTGATGGAGGACCCCGGACCACGACTAAATT	RFC2-2-R	73,249,990	TTAGTAAGGCAGGCAAGGGCTGTTCAGGTGGGAGCTCTAGATTGGATCTTGCTGGCAC
RFC2-3	116	RFC2-3-F	73,301,458	GGGTTCCCTAAGGGTTGGAGCTGTTTGCATCTCCGTCACCTCTGACCCCTGCATTC	RFC2-3-R	73,301,531	CACCCACAGCACACACAGATCAATACAGCTGGCCGGATCTAGATTGGATCTTGCTGGCAC
RFC2-4	120	RFC2-4-F	73,354,321	GGGTTCCCTAAGGGTTGGACAGCGTTGGACCTTTTTTTGTGGCTGGTGGTTCTGAGCA	RFC2-4-R	73,354,398	TGCCAACTCTGTGTGTGTGTCTAGCTCCCGCGAGACAGATCTAGATTGGATCTTGCTGGCAC
RFC2-5	124	RFC2-5-F	73,332,023	GGGTTCCCTAAGGGTTGGATGTCCTCCCACCCGGATAGTCACAGATGACGTTTGCAAGTG	RFC2-5-R	73,332,104	TGACACAGTCCCGTGGAAATTCCTGGTGCATGAGTCAGCTTTCTAGATTGGATCTTGCTGGCAC
RFC2-6	128	RFC2-6-F	73,301,177	GGGTTCCCTAAGGGTTGGAGGCAAGGCTTCGCATACAACCCAATGCTGAGAAAGGTTGTTTC	RFC2-6-R	73,301,262	TGTAACAATTCTCAATGCAGAGCACCCGCCCCCCTACAGGTCTTCTAGATTGGATCTTGCTGGCAC
RFC2-7	132	RFC2-7-F	73,299,009	GGGTTCCCTAAGGGTTGGATTCCTCACAACGTCAATGCCCCTGAAAGAATGACAGGTTTTTACT	RFC2-7-R	73,299,098	GGCACCTTCTGAGACCAATTCAGTTGCCTTCACAAGGACTTTTAATCTAGATTGGATCTTGCTGGCAC

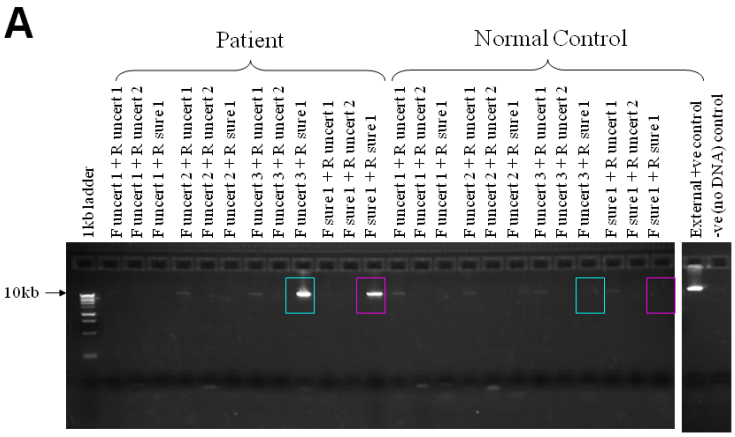
Supp. Data

FISH Cytogenetic Diagnoses

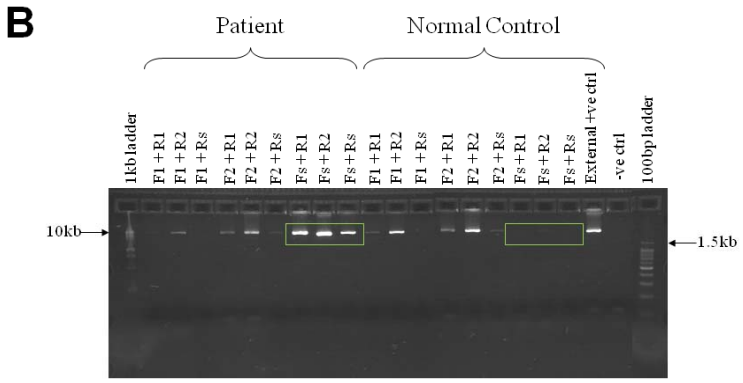
Case No.	FISH Diagnosis
3	nuc ish 21q22.11q22.12(RP11-79A12)x3
4	nuc ish 3p26.1(RP11-1017D24x3)pat ish del(X)(p22.13p22.13)(RP11-558P14-)[12]/Xp22.13(RP11-558P14dim)[38]dn
5	nuc ish Xp22.31(RP11692P14x2)
9	ish del(2)(q24.3q24.3)(RP11-454K9dim)dn nuc ish Xp22.31(RP11-483M24x3)mat
10	ish del(9)(q34.11q34.11)(G248P86186C8-)dn
12	ish del(18)(q21.2q21.2)(RP11-111C17-)[32]/18q21.2(RP11-111C17x2)[168]
13	ish del(X)(p21.2p21.2)(G248P88443C2-)[112]/ Xp21.2(G248P88443C2x1)[88]
20	ish del(10)(q21.3q21.3)(RP11-715K5-)pat
27	ish del(3)(p14.1p14.1)(G248P84614D2dim)



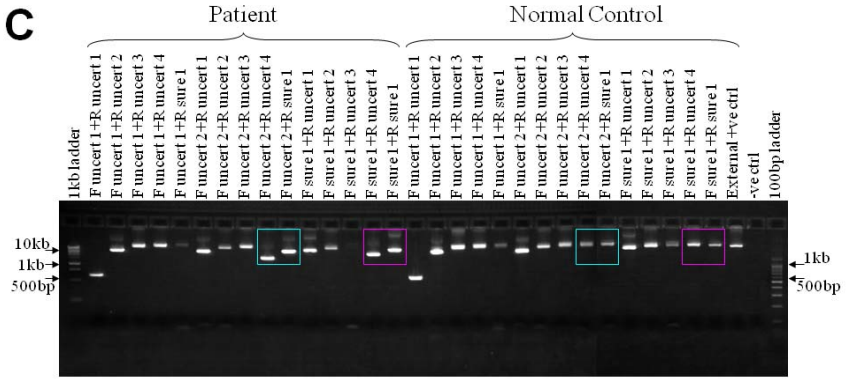
Supp. Figure S1. PCR confirmation of intragenic copy number changes. Intragenic deletions in: **a**. *DLG3* (case 30), and **b.** *SLC1A1* and *MCCC1* (case 17) were verified by PCR. Colored boxes help to indicate PCR products amplified from patient DNA but not from control DNA.



Case 31 (*NRXN1* deletion)

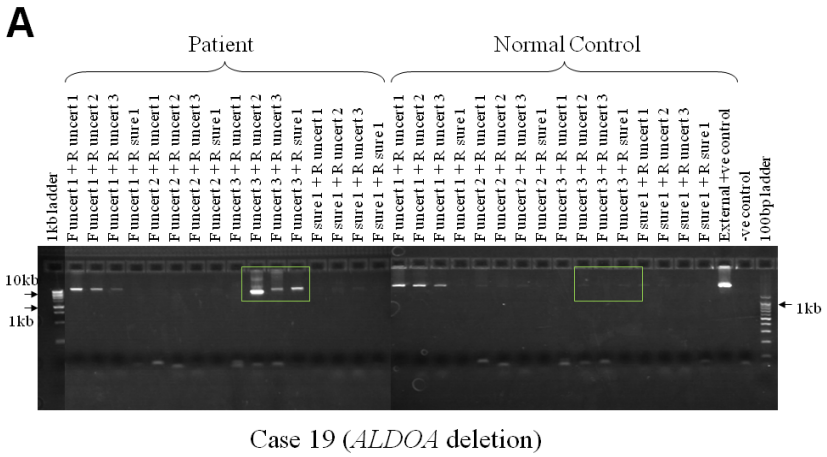


Case 11 (*NRXN1* deletion)

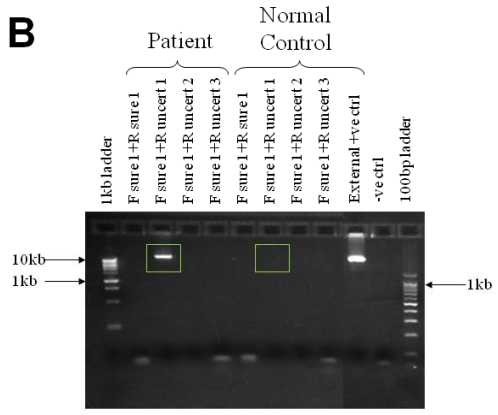


Case 18 (*CNTNAP2* deletion)

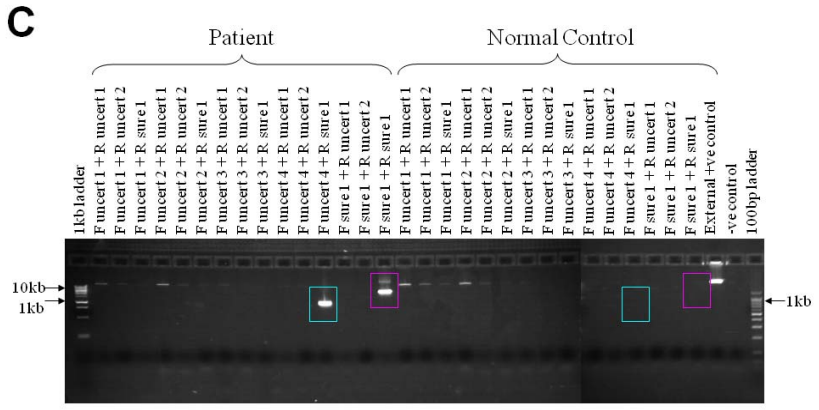
Supp. Figure S2. PCR confirmation of intragenic copy number changes. Intragenic deletions in: **a.** *NRXN1* (case 31), **b.** *NRXN1* (case 11), and **c.** *CNTNAP2* (case 18) were verified by PCR. Colored boxes help to indicate PCR product(s) amplified from patient DNA but not from control DNA.



Case 19 (*ALDOA* deletion)

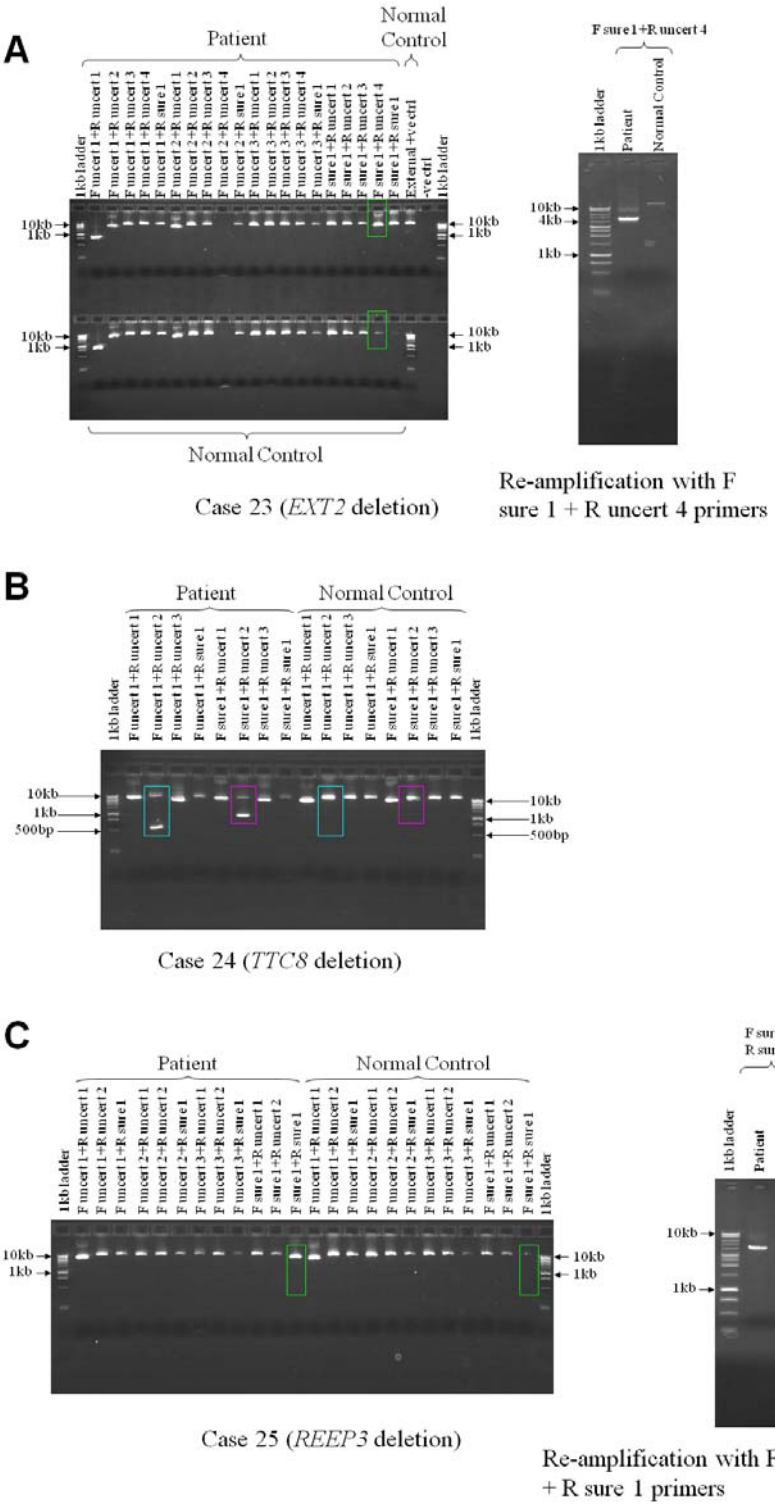


Case 21 (*FHIT* gain)

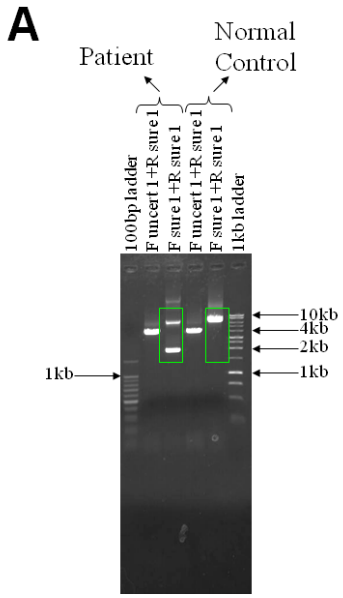


Case 22 (*TEK* deletion)

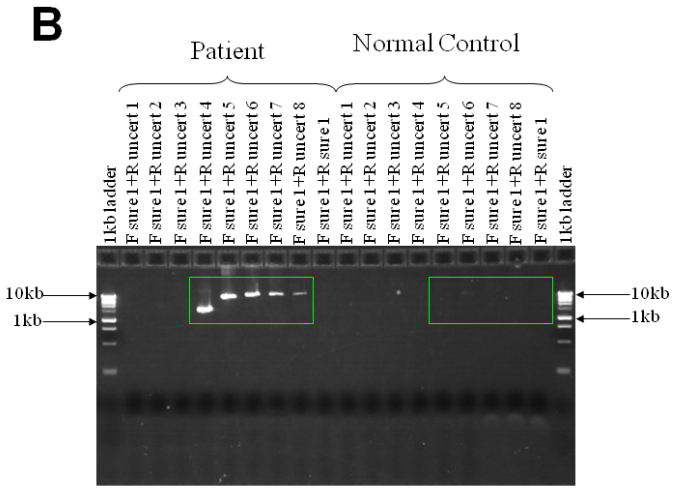
Supp. Figure S3. PCR confirmation of intragenic copy number changes. **a.** An intragenic deletion in *ALDOA* (case 19) was verified by PCR. **b.** An tandem, intragenic copy-number gain in *FHIT* (case 21) was verified by PCR. **c.** An intragenic deletion in *TEK* (case 22) was verified by PCR. Colored boxes help to indicate PCR product(s) amplified from patient DNA but not from control DNA.



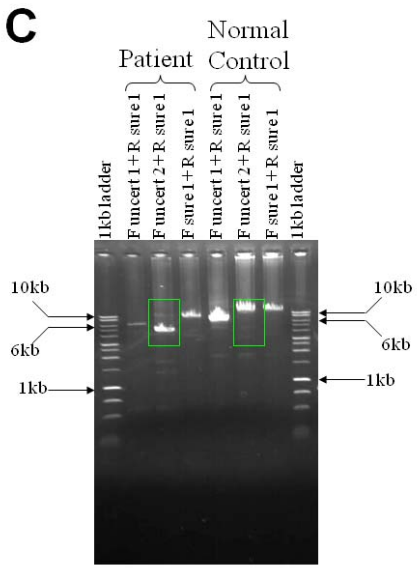
Supp. Figure S4. PCR confirmation of intragenic copy number changes. Intragenic deletions in: **a.** *EXT2* (case 23), **b.** *TTC8* (case 24), and **c.** *REEP3* (case 25) were verified by PCR. In some cases, colored boxes help to indicate PCR products amplified from patient DNA but not from control DNA.



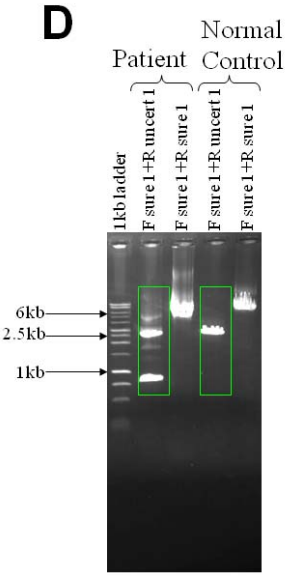
Case 26 (*MSH6* deletion)



Case 28 (*KIF7* deletion)

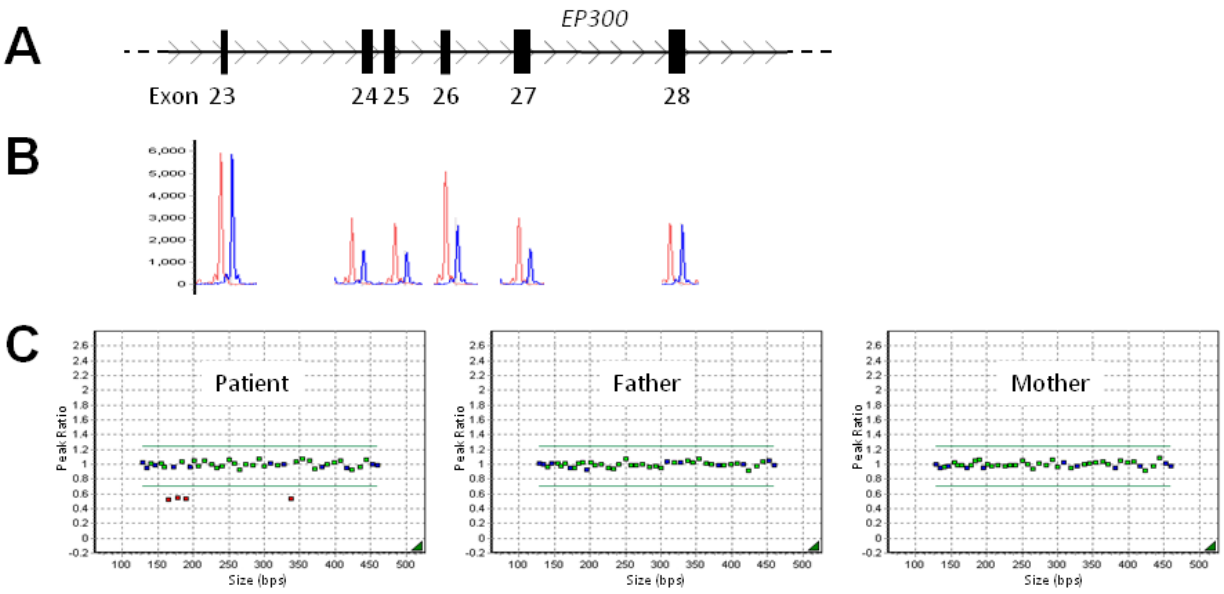


Case 29 (*KIF1B* deletion)

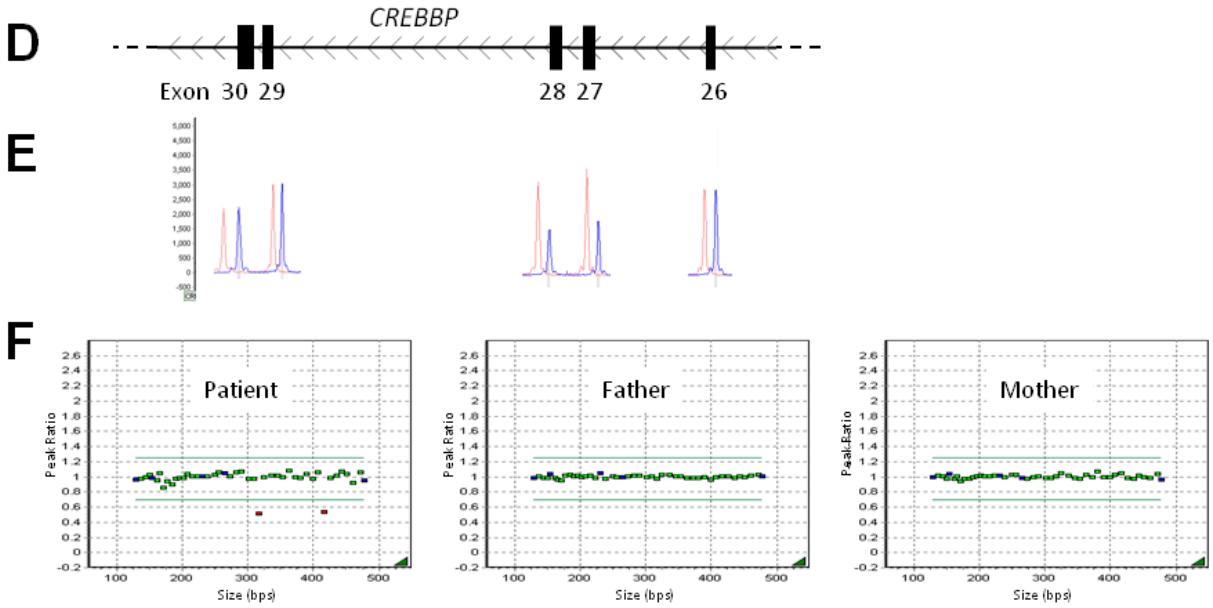


Case 15 (*JAG1* deletion)

Supp. Figure S5. PCR confirmation of intragenic copy number changes. Intragenic deletions in: **a.** *MSH6* (case 26), **b.** *KIF7* (case 28), **c.** *KIF1B* (cases 29), and **d.** *JAG1* (case 15) were verified by PCR. In some cases, colored boxes help to indicate PCR products amplified from patient DNA but not from control DNA.



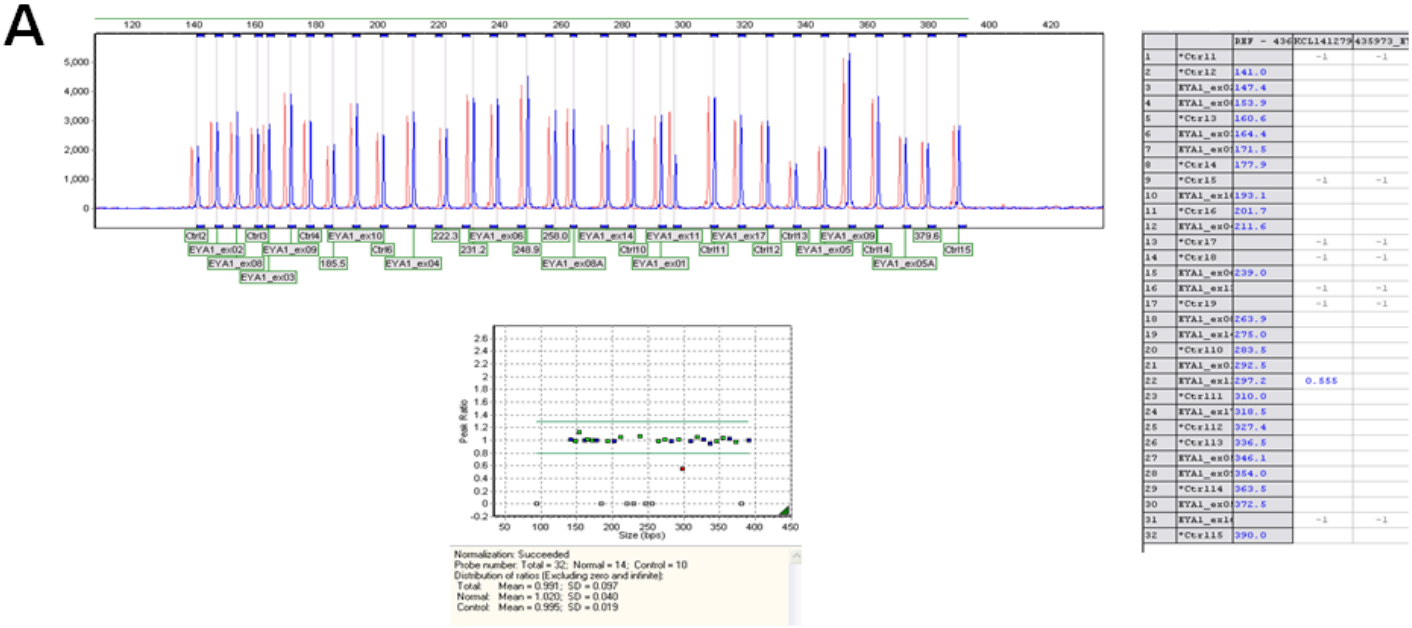
Case 3 (*EP300* deletion)



Case 5 (*CREBBP* deletion)

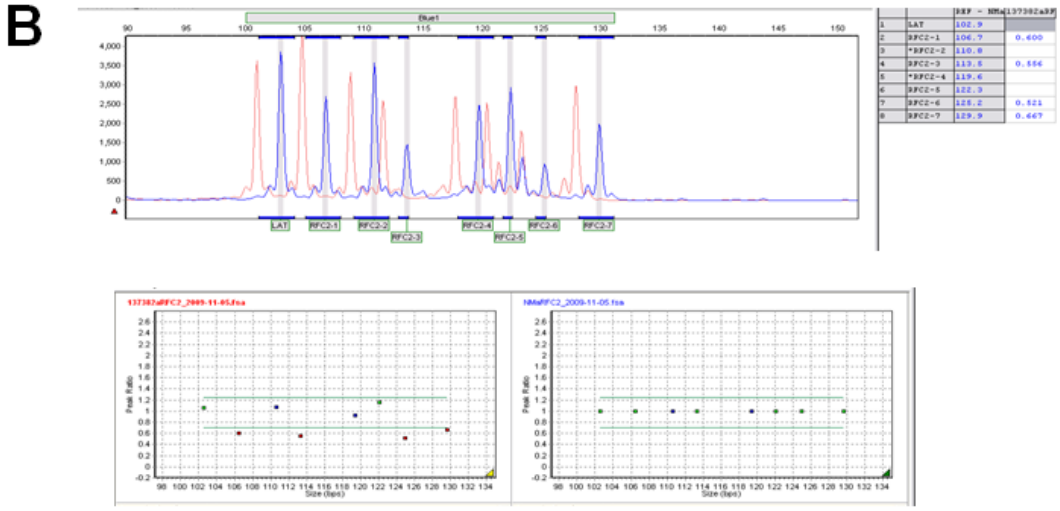
Supp. Figure S6. MLPA confirmation of intragenic copy number changes. Intragenic deletions in: **a-c.** *EP300* (case 3) and **d-f.** *CREBBP* (case 5) were verified by MLPA. **a-b, d-e.** MLPA traces aligned to local genomic maps of the genes interrogated. Control traces are in red, patient traces in blue. **c, f.** Dot plots displaying normalized MLPA results in which green probes interrogate exons of the genes of interest, blue probes are controls, and red probes indicate copy change.

A



Case 14 (*EYA1* deletion)

B



Case 16 Control

Case 16 (*RFC2* deletion)

Supp. Figure S7. MLPA confirmation of intragenic copy number changes. Intragenic deletions in: **a.** *EYA1* (case 14) and **b.** *RFC2* (case 16) were verified by MLPA. Control traces are in red, patient traces in blue. Dot plots displaying normalized MLPA results are also displayed, in which green probes interrogate exons of the gene of interest, blue probes are controls, and red probes indicate copy change.

Supp. Table S1. Complete listing of gene-containing CNVs

All gene-containing copy number variations (CNVs) for each case are listed. Known benign CNV may be omitted. Exon numbers are based on the longest RefSeq transcript listed in the UCSC Genome Browser, with the exception of *CDKL5*, for which exon numbering is as in [Erez *et al.*, 2009].

Case No.	Genes in CNV	Chromo-somal Location	Loss/Gain	De novo vs. Inherited	Exons	Micro RNAs in region	Size (range unless confirmed by sequencing; Mb unless otherwise specified)	Min Interval	Max Interval	Mean Log_2	Median Log_2	No. Probes
1	*MECP2*	Xq28	Loss (in a female)	De novo	Exons 3 and 4 (partial) of 4.	No	0.002-0.002	152949428-152951487	152949386-152951490	-0.5	-0.35	25
2	*PTEN*	10q23.31	Loss	Not maternally inherited	Exons 3-5 of 9	No	0.008-0.026	89675297-89683063	89675267-89701622	-0.75	-0.87	14
3	*EP300*	22q13.2	Loss	De novo	Exons 24-27 of 31	No	0.002-0.005	39894352-39896594	39892913-39898247	-0.83	-0.83	13
" "	*KCNE1*	21q22.11-q22.12	Gain	Inherited, maternally	Whole gene	No	0.163-0.207	34657921-34821194	34625313-34832077	0.45	0.382	65
" "	*KCNE2*	" "	" "	" "	Whole gene	" "	" "	" "	" "	" "	" "	" "
" "	*FAM165B*	" "	" "	" "	Whole gene	" "	" "	" "	" "	" "	" "	" "
" "	*RCAN1*	" "	" "	" "	Whole gene, or exons 3-4 of 4, depending on the splice variant	" "	" "	" "	" "	" "	" "	" "
" "	*Unnamed transcript*	" "	" "	" "	Whole gene	" "	" "	" "	" "	" "	" "	" "
4	*CDKL5*	Xp22.13	Loss (in a male; mosaic; FISH showed del in 24% (12/50) of cells)	De novo	Exons 1-3 of 21 (exon numbering as in Erez *et al.*, 2009).	No	0.105-0.128	18343025-18447902	18331857-18460326	-0.43	-0.43	28
" "	*GRM7*	3p26.1	Gain	Inherited, paternally	Exon 1 of 11	No	0.765-0.795	6174990-6939651	6155310-6949832	0.55	0.56	40
" "	*Unnamed transcript*	" "	" "	" "	Whole gene	" "	" "	" "	" "	" "	" "	" "
5	*CREBBP*	16p13.3	Loss	De novo	Exons 27-28 of 31	No	0.001-0.002	3726517-3727028	3726327-3728439	-0.43	-0.5	10
" "	*PNPLA4*	Xp22.31	Gain (in a male)	Inherited, maternally	Whole gene	Yes (listed as one of the gained genes).	0.248-0.358	7827298-8075153	7801179-8159482	0.96	0.9	14
" "	*has-mir-651*	" "	" "	" "	Whole miRNA	" "	" "	" "	" "	" "	" "	" "
" "	*VCX2*	" "	" "	" "	Whole gene	" "	" "	" "	" "	" "	" "	" "
6	*ZDHHC9*	Xq25	Loss (in a male)	Inherited, maternally	Exons 10-11 of 11	No	0.006-0.031	128766911-128772552	128741846-128772723	-1.27	-0.98	10
" "	*SASH3*	" "	" "	" "	Exons 2-8 of 8	" "	" "	" "	" "	" "	" "	" "
7	*FAM58A*	Xq28	Loss (in a female)	De novo	Exon 5 of 5	No	0.001-0.016	152506268-152507325	152494741-152510848	-0.64	-0.53	5
" "	*ATP2B3*	" "	" "	" "	Exon 21 of 21	" "	" "	" "	" "	" "	" "	" "
8	*HPRT1*	Xq26.2	Loss (in a male)	Inherited, maternally	Exon 9 of 9	No	502bp (by sequencing)	ChrX:133461536-133462037		-2.48	-2.26	3

Case No.	Genes in CNV	Chromo-somal Location	Loss/Gain	De novo vs. Inherited	Exons	Micro RNAs in region	Size (range unless confirmed by sequencing; Mb unless otherwise specified)	Min Interval	Max Interval	Mean Log_2	Median Log_2	No. Probes
9	*SCN3A*	2q24.3	Loss	De novo	Exon 1 of 28	No	0.094-0.121	165768300-165862069	165751604-165872284	-0.75	-0.89	26
" "	*SCN2A*	" "	" "	" "	Exon 1-3 of 27	" "	" "	" "	" "	" "	" "	" "
" "	*VCX3A/VCX2*	Xp22.31	Gain (in a female)	Inherited, maternally	Whole gene	Yes (listed as one of the gained genes).	1.786-1.870	6289260-8075153	6289091-8159482	0.46	0.49	95
" "	*HDHD1A*	" "	" "	" "	Whole gene	" "	" "	" "	" "	" "	" "	" "
" "	*STS*	" "	" "	" "	Whole gene	" "	" "	" "	" "	" "	" "	" "
" "	*VCX/VCX2*	" "	" "	" "	Whole gene	" "	" "	" "	" "	" "	" "	" "
" "	*VCX2*	" "	" "	" "	Whole gene	" "	" "	" "	" "	" "	" "	" "
" "	*PNPLA4*	" "	" "	" "	Whole gene	" "	" "	" "	" "	" "	" "	" "
" "	*has-mir-651*	" "	" "	" "	Whole miRNA	" "	" "	" "	" "	" "	" "	" "
10	*STXBP1*	9q34.11	Loss	De novo	Exons 1-4 of 20	No	0.047-0.086	129414011-129460757	129375646-129461836	-0.73	-0.76	16
" "	*FAM129B*	" "	" "	" "	Exon 1 of 14	" "	" "	" "	" "	" "	" "	" "
" "	*COMT*	22q11.21	Loss	Inherited, maternally	Exon 1 of 6	No	0.010-0.019	18309472-18319136	18309090-18328444	-0.64	-0.61	7
" "	*TXNRD2*	" "	" "	" "	Exon 1 of 18	" "	" "	" "	" "	" "	" "	" "
11	*NRXN1*	2p16.3	Loss	Inherited, paternally	Exons 17-18 of 24	No	17121 bp (by sequencing)	Chr2:50539661-50556784 (inclusive of 3bp microhomology)		-1	-1.04	7
12	*TCF4*	18q21.2	Loss (mosaic; FISH showed del in 16% (32/200) of cells)	Unknown	Exons 3-8 of 20	No	0.185-0.205	51118120-51302634	51108121-51312629	-0.54	-0.52	35
13	*IL1RAPL1*	Xp21.2	Loss (in a male; mosaic; FISH showed del in 56% (112/200) of cells)	Unknown	Exons 7-9 of 11	No	0.035-0.058	29835047-29870211	29824737-29882319	-0.98	-1.02	13
14	*EYA1*	8q13.3	Loss	Inherited, maternally	Exon 12 of 18	No	0.000-0.027	72,319,254-72,319,695	72,305,679-72,332,204	-1.03	-1.03	4
" "	*CHRNA7*	15q13.3	Gain	Inherited, maternally	Exons 1-4 of 10	No	0.150-0.716	30,083,430-30,233,204	29,517,737-30,233,287	0.5	0.49	25
" "	*OTUD7A*	" "	" "	" "	Whole gene	" "	" "	" "	" "	" "	" "	" "
15	*JAG1*	20p12.2	Loss	De novo	Exons 6-8 of 26	No	.001-.006	10,579,979-10,581,413	10,579,088-10,584,793	-0.62	-0.73	9
16	*RFC2*	7q11.23	Loss	Inherited, paternally	Exons 1-5 of 11	No	0.023-0.046	73298702-73321373	73295832-73341361	-0.68	-0.79	17
17	*SLC1A1*	9p24.2	Loss	Inherited, paternally	Exon 1 of 12	No	0.073-0.129	4418574-4491934	4372543-4501065	-0.76	-0.87	9
" "	*MCCC1*	3q27.1	Loss	Inherited, paternally	Exons 2-3 of 19	No	0.002-0.008	184292729-184295167	184287564-184295402	-0.9	-0.97	7
18	*CNTNAP2*	7q35	Loss	Unknown	Exon 8 of 24	No	9958 bp (by sequencing)	Chr7:146458392-146468351 (inclusive of 2bp microhomology)		-0.79	-0.77	4

Case No.	Genes in CNV	Chromo-somal Location	Loss/Gain	De novo vs. Inherited	Exons	Micro RNAs in region	Size (range unless confirmed by sequencing; Mb unless otherwise specified)	Min Interval	Max Interval	Mean Log_2	Median Log_2	No. Probes
19	*ALDOA*	16p11.2	Loss	Unknown	Exon 1-4 of 14	No	13,885 bp (by sequencing)	Chr16: 29,961,204-29,975,150 (inclusive of 62bp homology)		-0.64	-0.63	18
" "	X Chromosome (Klinefelter's)	Whole chromosome	Gain	Unknown	-	-	Whole Chromosome			0.76	0.84	13,040
20	*CTNNA3*	10q21.3	Loss	Inherited, paternally	Exons 10-11 of 18	No	0.101-0.367	67950370-68051567	67809125-68176504	-0.95	-1.01	6
21	*FHIT*	3p14.2	Gain	Inherited, paternally	Exon 4 of 10	No	17,936 bp (by sequencing)	chr3:60,779,651-60,797,586 (exact)		0.83	0.89	6
" "	*Unnamed transcript*	3q13.11	Loss	Inherited, paternally	Whole transcript	No	0.460-0.555	105005505-105465469	104945375-105499895	-0.69	-0.68	13
22	*TEK*	9p21.2	Loss	Unknown	Exons 3-9 of 23	No	29,964b bp (by sequencing)	Chr9:27150274-27180241 (inclusive of 4bp microhomology)		-0.53	-0.61	27
23	*EXT2*	11p11.2	Loss	Unknown	Exon 12 of 16	No	0.001-0.022	44,184,602-44,185,360	44,176,244-44,197,768	-0.85	-0.82	5
24	*TTC8*	14q31.3	Loss	Unknown	Exons 3-6 of 14	No	0.004-0.013	88,376,567-88,380,220	88,375,994-88,388,896	-0.78	-0.87	9
25	*REEP3*	10q21.3	Loss	Inherited, paternally	Exons 7-8 of 8	No	0.003-0.018	65,048,965-65,052,014	65,040,526-65,058,056	-0.87	-0.9	13
26	*MSH6*	2p16.3	Loss	Unknown	Exons 4-10 of 10	No	0.004-0.006	47,884,010-47,887,581	47,881,791-47,887,705	-0.81	-0.8	15
" "	*FBXO11*	" "	" "	" "	Exon 23 of 23	" "	" "	" "	" "	" "	" "	" "
27	*FOXP1*	3p14.1	Loss	Unknown	Exons 14-21 of 21	No	0.029-0.030	71090495-71119790	71090029-71119919	-0.49	-0.54	27
28	*KIF7*	15q26.1	Loss	Inherited, paternally	Exons 1-2 of 19	No	.003-.032	87997345-88000145	87996808-88028535	-0.96	-1.04	4
" "	*PLIN1*	" "	" "	" "	Whole gene	" "	" "	" "	" "	" "	" "	" "
" "	*PEX11A*	" "	" "	" "	Exon 3 of 3	" "	" "	" "	" "	" "	" "	" "
29	*KIF1B*	1p36.22	Loss	Inherited, paternally	Exons 37-41 of 47	No	.005-.012	10,343,400-10,348,260	10,335,800-10,348,286	-0.64	-0.62	16
" "	*TAAR2*	6q23.2	Gain	Unknown	Whole gene	Yes (among the listed genes)	0.293-0.416	132,984,448-133,277,043	132,959,124-133,374,834	0.67	0.65	5
" "	*TAAR1*	" "	" "	" "	Whole gene	" "	" "	" "	" "	" "	" "	" "
" "	*VNN1*	" "	" "	" "	Whole gene	" "	" "	" "	" "	" "	" "	" "
" "	*VNN3*	" "	" "	" "	Whole gene	" "	" "	" "	" "	" "	" "	" "
" "	*VNN2*	" "	" "	" "	Whole gene	" "	" "	" "	" "	" "	" "	" "
" "	*Unnamed transcript*	" "	" "	" "	Whole gene	" "	" "	" "	" "	" "	" "	" "
" "	*RPS12*	" "	" "	" "	Whole gene	" "	" "	" "	" "	" "	" "	" "
" "	*SNORD101*	" "	" "	" "	Whole gene	" "	" "	" "	" "	" "	" "	" "
" "	*SNORD100*	" "	" "	" "	Whole gene	" "	" "	" "	" "	" "	" "	" "
" "	*SNORA33*	" "	" "	" "	Whole gene	" "	" "	" "	" "	" "	" "	" "
30	*DLG3*	Xq13.1	Loss (in a female)	Inherited, maternally	Intron 18.	No	1099 bp (by sequencing)	ChrX:69637575-69638673		-0.79	-0.83	3
31	*NRXN1*	2p16.3	Loss	Not maternally inherited	Intron 3 of 23 (introns)	No	30,792 bp (by sequencing)	Chr2:51072619-51103413 (inclusive of 3bp microhomology)		-0.83	-0.8	3

Supp. Table S2. Results of DNA sequencing at deletion and duplication breakpoints

Case No.	Gene	Size (bp) and CNV type	Sequence	Features	Repetitive elements at Breakpoint[a]		Predicted molecular consequence
					Left	Right	
8	*HPRT1*	502 del	L: **AACAAATTAAACTA**ATGTGATAGACTACTGCTTTGTTTTCAAAAGA S: **AACAAATTAAACTA**CTGCTTTTACTACTGTAA**ACTATTGAGTGAAA** R: TTGTAAATGAAAAAATTCTCTTAAACCACAGC**ACTATTGAGTGAAA**	18 bp insertion; 7 flanking repeated bp	-	-	Del of coding region of final exon
11	*NRXN1*	17,121 del	L: **TATTAGCACTGAA**ATATGTTGAT S: **TATTAGCACTGAACATGTACAAT** R: AAGAAGTAGA**GAACATGTACAAT**	3 bp micro-homology	-	-	In-frame del of coding exons
18	*CNTNAP2*	9,958 del	L: **TAGGAGGATCAC**TTGAGCCCAC S: **TAGGAGGATCACAACCTGCTGC** R: CCCTAGACGT**ACAACCTGCTGC**	2 bp micro-homology	*Alu*Jo (+)	-	Frameshift and premature termination codon
19	*ALDOA*	13,885 del	L: **CACCACCACACCCAGCTAAT...GGCTGGTCTC**AAACTCCTGA S: **CACCACCACACCCAGCTAAT...GGCTGGTCTCGAACTCCTGA** R: TGCCACCACG**CCCAGCTAAT...GGCTGGTCTCGAACTCCTGA**	62 bp homology	*Alu*Sq (-)	*Alu*Sx (-)	Del of multiple 5' UTR exons in some splice variants
21	*FHIT*	17,936 gain	L: **CTATCTTGGG**TCTCAGTCTA S: **CTATCTTGGGAAATGGGAAA** R: AAAAGTTGTA**AAATGGGAAA**	No micro-homology	L1ME b (-)	LTR3 8B (-)	Gain of a 5' UTR exon
22	*TEK*	29,964 del	L: **CCTCCCACTATGGC**CTCTCAAAGT S: **CCTCCCACTATGGCTGGTCACGAT** R: ACTCAAGGCC**TGGCTGGTCACGAT**	4 bp micro-homology	*Alu*Jo (-)	L2 (-)	In-frame del of coding exons
30	*DLG3*	1,099 del	L: **GTAAGACTCC**TG CTGCCCTGCGGGGGG S: **GTAAGACTCC**AT ACTCC**ATTGCTGGGT** R: TTGTTGGGAGAG GCAGG**ATTGCTGGGT**	7 bp insertion / 7 tandem repeated bp	-	-	Intronic del; possible intron retention owing to small intron size
31	*NRXN1*	30,792 del	L: **AGGTCTGGATCAA**CAGTGTGTAC S: **AGGTCTGGATCAAAATATTTTCC** R: CAAGCACCTA**CAAAATATTTTCC**	3 bp micro-homology	-	-	Intronic del

[a] Obtained from the UCSC Genome Browser.

del = deletion; L = "left" breakpoint region; S = sequenced fragment; R = "right" breakpoint region; bold text = perfect homology to sequenced PCR product; solid underline = microhomology; dotted underline = duplicated sequences; (+) = "forward" orientation with respect to the reference sequence; (-) = reverse orientation with respect to the reference sequence.