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Supplemental Data

Haploinsufficiency of *HDAC4* Causes Brachydactyly Mental Retardation Syndrome, with Brachydactyly Type E, Developmental Delays, and Behavioral Problems

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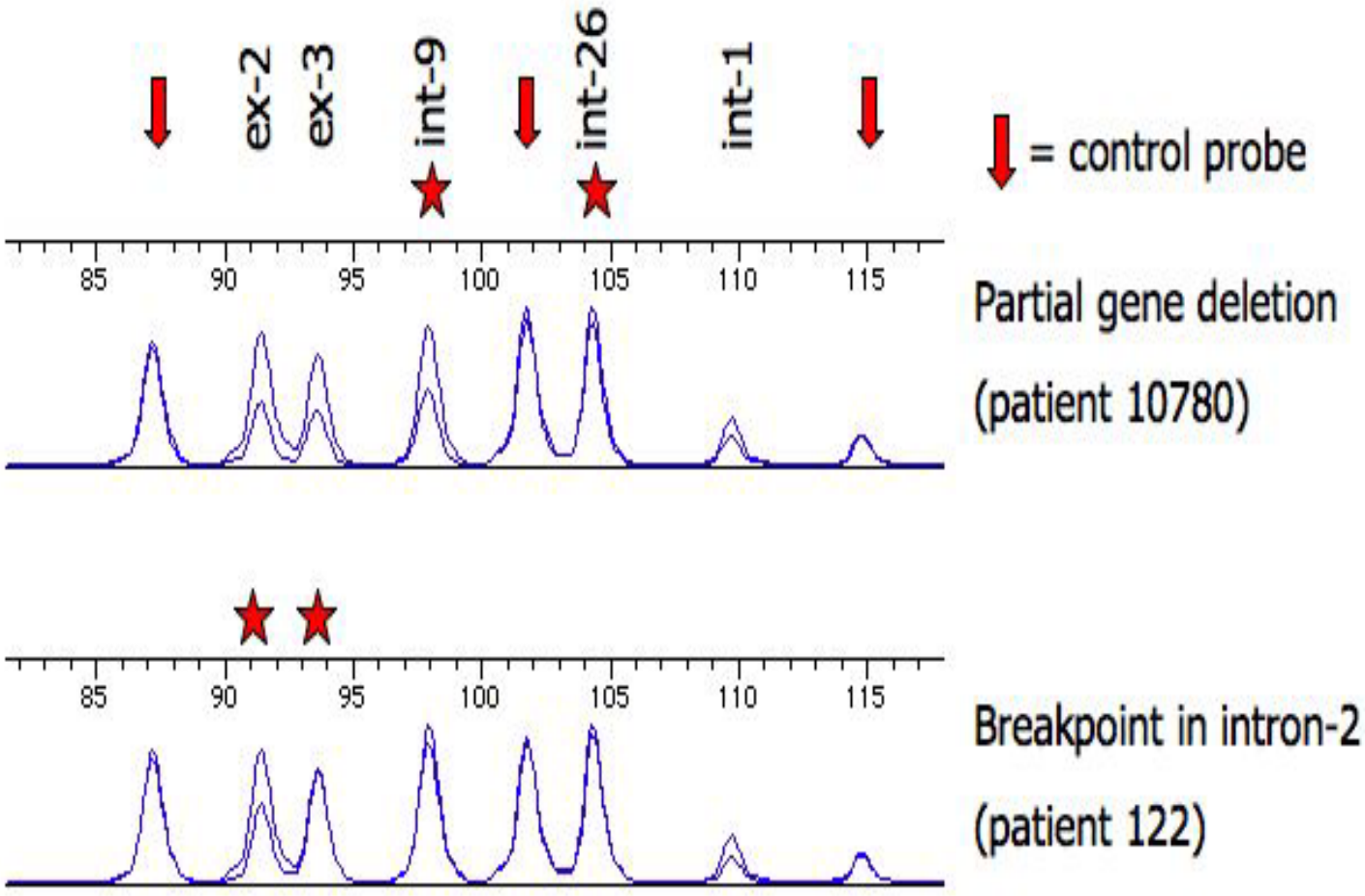

Figure S1. MLPA analysis of *HDAC4* deletion breakpoints in key 2q37.3 deletions. *Top:* Analysis of patient 10780 showed an *HDAC4* deletion extending at least through intron 9 but the breakpoint occurring prior to intron 26. *Bottom:* Patient 122 revealed a deletion including intron 1 and exon 2, with the breakpoint occurring between the probes for exon 2 and exon 3. Stars indicate regions between which the breakpoint occurs for each case. Control probes are indicated by the arrows and show 2 alleles of equal intensity for each.

Table S1. *HDAC4* amplification and sequencing oligonucleotides.

Exon	Primer	Primer Sequence	Tm (C)	Amplicon
1	1F	GGCTCGGCGCTTGAACGTCT	64	220
1	1R	TGGGCAAAGAAAGCCCCGCT	64	
2	2F	TGCGCGCAGTTTCTGAAGCC	64	214
2	2R	CCCCTCGCCCTCTCTGCACT	64	
3	3F	CCAGGGACAGCAAAGGGCGG	66	376
3	3R	CGGAGGCAGGGCTGGAGTCA	66	
4	4F	AGCCCGGAATGGCCCTGACT	63	654
4	4R	TACTCCCCGTGTGCTGCCCC	63	
5	5F	TAGCCGTCCCCAGCCCTTCC	64	412
5	5R	CTGCCGCACGAGTGTACCCC	64	
6	6F	GGGGCAGTGCGCTGGGTAAA	64	285
6	6R	CTGCAGGTGATTCCTTCTCTAAGTGG	64	
7	7F	TGAGCTCCCTGCGCTCTCCC	64	400
7	7R	GGGGGTTGACAGCGTGAGGC	64	
8	8F	GGGCATTCGGGCCACAGGTC	64	320
8	8R	AGGCCACTTTCCCTCACCCCA	64	
9	9F	ATGTTTGGCCGTGACAGACT	60	219
9	9R	AAGGACCCATCACCACCAC	60	
10	10F	AGCATCCTGGCTGTGCTTT	58	242
10	10R	CCAGGCCCATTTGTGCTC	58	
11	11F	TTCCCCTCTGCTGTTTCTTC	58	398
11	11R	GTTCCCTCTTTCTGCCTCCT	58	
12	12F	GACCCAGCTCTCTGTGCTTC	60	377
12	12R	ACCACAGAAGATGCCACCTG	60	
13	13F	CAACACGGCCGTTTCTTC	60	243
13	13R	ACCCTCAGGCTGCACAAA	60	
14	14F	ATGACACGCTGATGCTGAAG	58	237
14	14R	TAAGCCCAAAGAACCACCTG	58	
15	15F	CTGTCTGTGGAGCTGAAGCA	60	222
15	15R	ACCCAATATGGGAGGAAAGG	60	
16	16F	CCTCGTTGTCCCACAAATG	58	220
16	16R	ACCACTGGGACTCGAGAAGA	58	
17	17F	TCACTGTGGGGTGTTGTTTC	58	232
17	17R	CAGCCTGATGAGAGGGAGAC	58	
18	18F	AGGGTGCAGCAAGAAACTGT	58	245
18	18R	CCTAAGGGAGGGAAGGAAGA	58	
19	19F	CTCCAGCGTCAGTTCTCTCC	60	223
19	19R	CCTAAGCTTCCCACATCCAA	60	
20	20F	TGCCTCAGCCCTGAAGTAGT	60	179
20	20R	GGCCCTTATATACCCCACCT	60	
21	21F	CGTGTGTTTCTCTCCTTCTGG	60	215
21	21R	GACACGCTCATCTCCAACAA	60	
22	22F	ACCCAGTAACGCCTTCTCCT	60	234
22	22R	TAAAAAGGGGACCTGACACG	60	
23	23F	TCTTACGATGCCATGAGACG	60	242
23	23R	GGGTCTCTGGGGTCTTCCTA	60	
24	24F	GTCTCGGAACACCCGTCTAA	60	240
24	24R	GTATAGGGGGACAGGGATGG	60	
25	25F	ACTTTCCTCACCCCACCAC	60	246
25	25R	GGTTCTGACCCTGAATAGTGTG	60	
26	26F	CACAGCCTTTAACCCACGTT	60	183
26	26R	TGGCTGAGCTTCAAGACAGA	60	

Table S2. *HDAC4* cDNA oligonucleotides for amplification and sequencing.

Coding exon (cDNA)	Primer	Sequence	Tm	Amplicon (bp)
1-8	cDNA 1F	GAGTTTGGAGCTCGTTGGAG	56	1135
1-8	cDNA 1R	AAGGATGGCGATGTGTAGAGG	56	
1-8	Sequencing Primer 1F	GCAGCTCAAGAACAAGGAG	NA	NA
1-8	Sequencing Primer 1R	CTCTTTGCCCTTCTCCTTGTTC	NA	NA

Table S3. MLPA probes for 2q37.3 and *HDAC4*.

Name	Sequence	Ensembl Build 41
rs870790A	**GGGTTCCCTAAGGGTTGGA**TTCTTAGGACCTGAAAGTCTGAACCAGCATTCCAA	239980739
rs870790B	GTGGGAGTATTGTTCAAGCGGTGATGGAATTG**TCTAGATTGGATCTTGCTGGCAC**	239980805
HDAC4-2A	**GGGTTCCCTAAGGGTTGGA**GAGGCTCGGCGCTTGAACGTCTG	239939431
HDAC4-2B	TGACCCAGCCCTCACCGTCCCGGTAC**TCTAGATTGGATCTTGCTGGCAC**	239939479
HDAC4-3A	**GGGTTCCCTAAGGGTTGGA**TGGCCGAGACCAGCCAGTGGAGCTG	239823237
HDAC4-3B	CTGAATCCTGCCCGCGTGAACCACAT**TCTAGATTGGATCTTGCTGGCAC**	239823287
HDAC4-i9A	**GGGTTCCCTAAGGGTTGGA**GCACTTGCCCTTCACTCTTCACCTTCCA	239726184
HDAC4-i9B	ATTTGGGGTGAGGGAAAGTGGCCTGTG**TCTAGATTGGATCTTGCTGGCAC**	239726238
HDAC4-i26A	**GGGTTCCCTAAGGGTTGGA**CTCCTTCCAGTGCCAAAGCCCCTTAGAGAC	239639900
HDAC4-i26B	GCATGAGGAGCATTAGATCCTGAACAGATGGA**TCTAGATTGGATCTTGCTGGCAC**	239639961