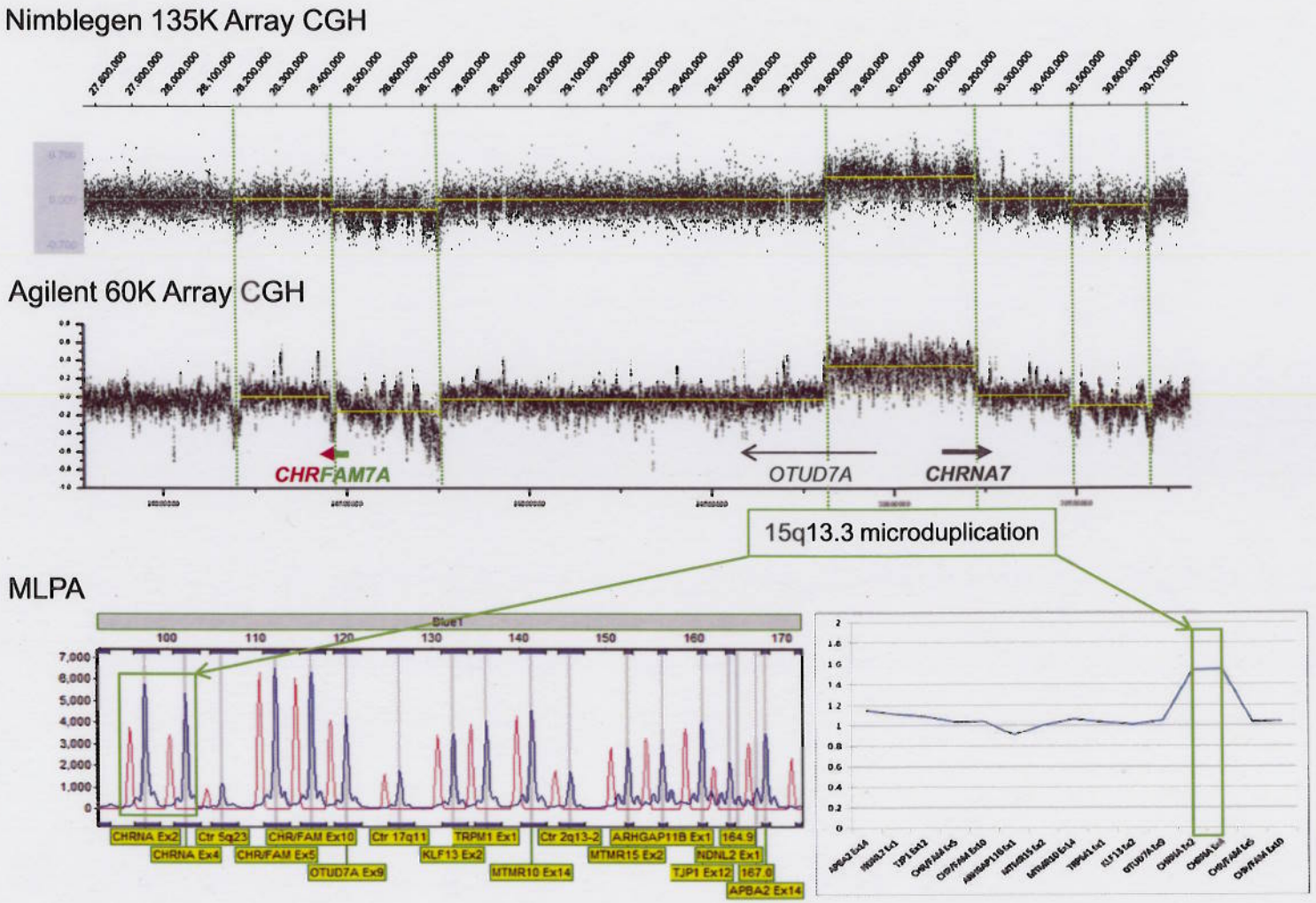
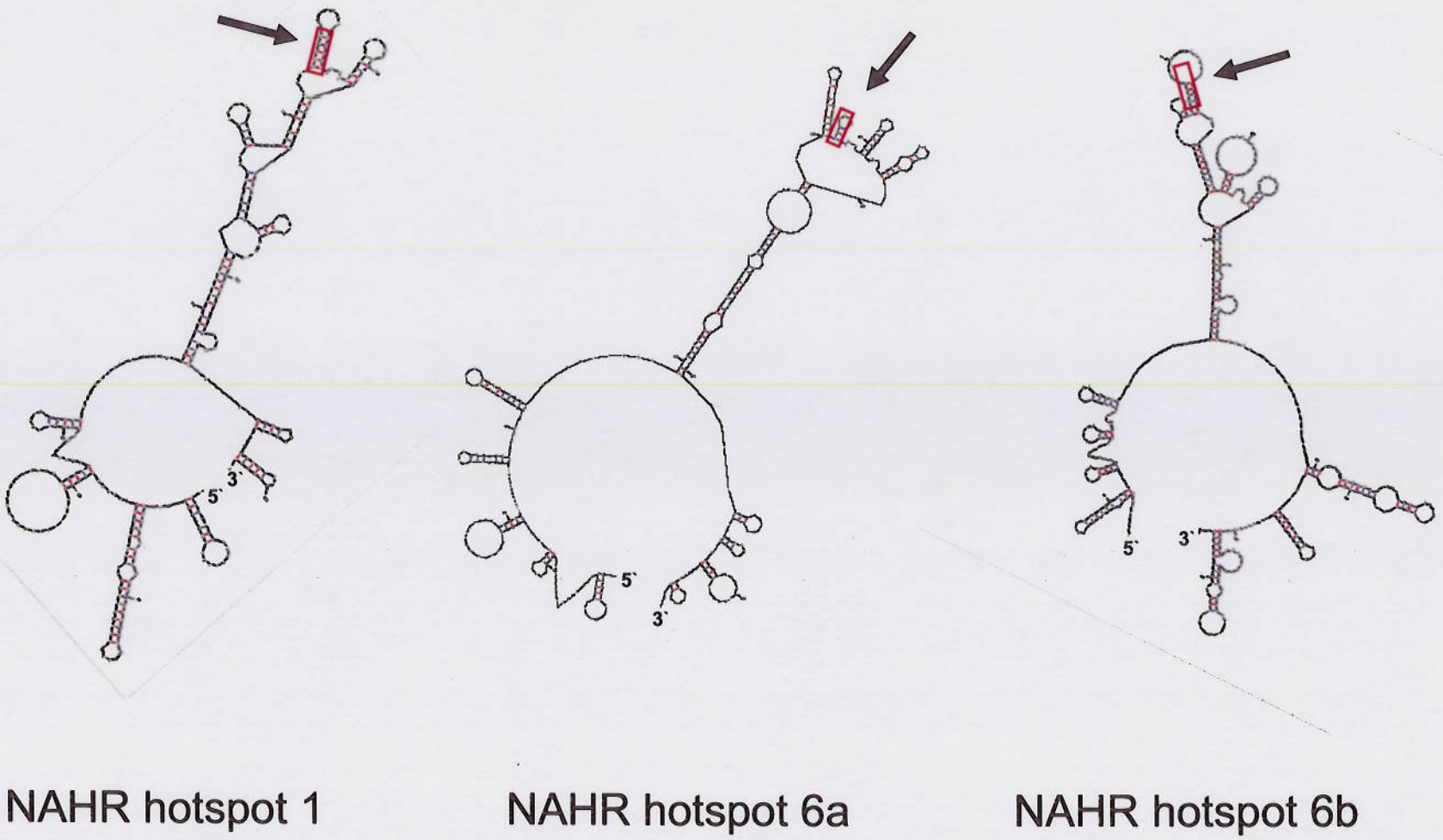
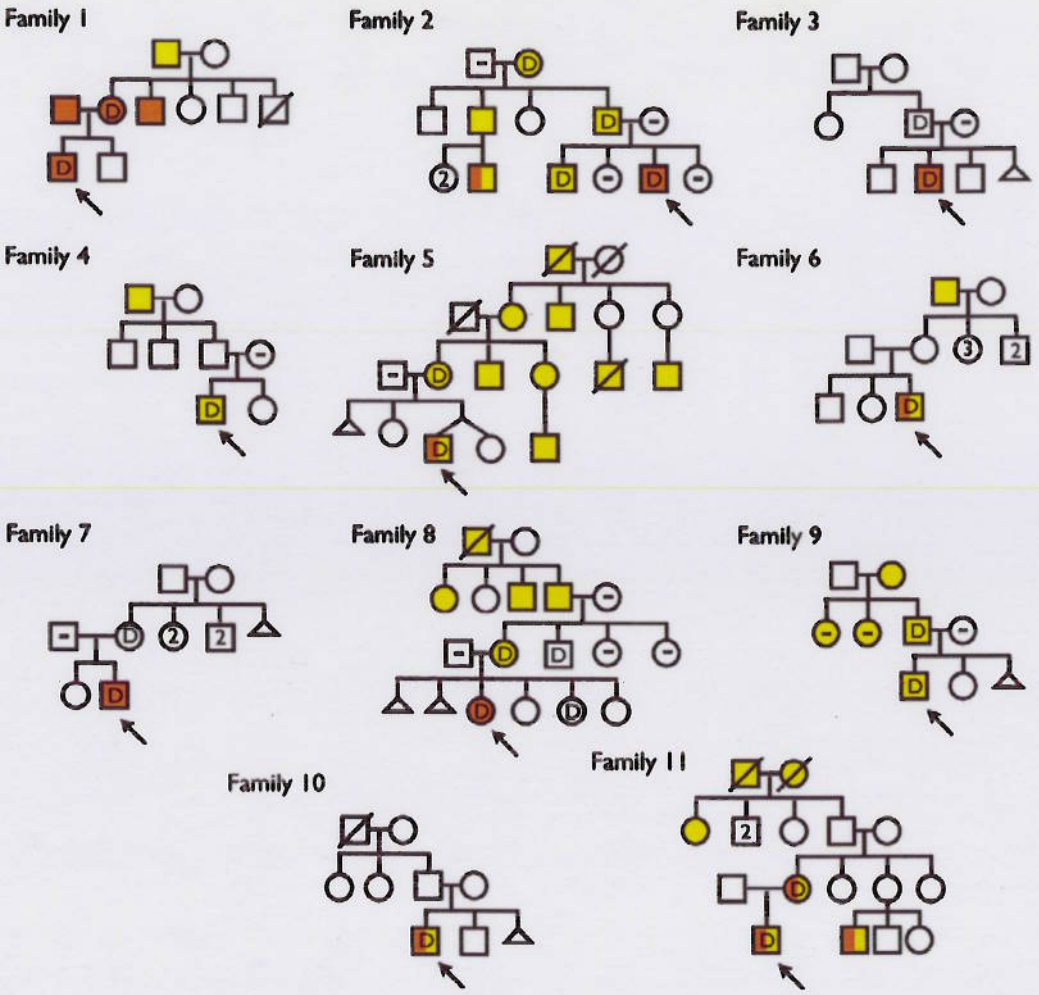


Supp. Figure S1. Comparison of Nimblegen aCGH, Agilent aCGH, and MLPA analyses of a case of 15q13.3 class 1 microduplication. The copy number of *CHRNA7* exons 1-4 is doubled. Exons 5-10 are not duplicated due to the presence of *CHRFAM7A* gene on a common ch15 (see Figures 1-2).



Supp. Figure S2. Secondary structures around NAHR breakpoint hotspots in CHRNA7-LCRs. Arrows point at imperfect copies of the CCTCCCT recombination-associated motif (framed).



Supp. Figure S3. Pedigree analyses of eleven unrelated index patients with microduplication of *CHRNA7*. Index patients are marked with an arrow. "D" indicates duplication of *CHRNA7*, whereas "-" depicts the individual tested negative for the presence of a microduplication of *CHRNA7*. Orange color encodes for developmental delay/learning deficits/mental retardation. Yellow color encodes for neuropsychiatric phenotypes.

Supp. Figure S3. Families

Family 1: This 2-year-old Hispanic boy has significant speech delay and severe pica, eating large amounts of non-nutritive substances including dirt, soil and sheetrock. His mother who carries the duplication has learning deficits. Family history is significant for a maternal uncle with mild mental retardation and the maternal grandfather with depression, aggressive behaviors and rage attacks. **Family 2:** The index patient is a 3-year-old male with hypotonia, developmental delay, and intestinal pseudo-obstruction. His 5-year-old brother carrying the microduplication has been diagnosed with bipolar disorder. Their father, paternal uncle, and paternal grandmother have a history of depression. A paternal cousin has autism and displays aggressive behaviors. **Family 3:** The index patient presented with severe global developmental delay, hypotonia, and seizure disorder. There is no family history of neuro-psychiatric disease. **Family 4:** The index patient is a 3-year-old male with global developmental delay and hypotonia. Both parents are phenotypically normal. The paternal grandfather is nicotine dependent. **Family 5:** The propositus has autism spectrum disorder and global developmental delay. There is a strong family history of heavy alcohol use in the mother, maternal aunt, and maternal uncle and alcoholism in the maternal grandmother, great-uncle, and great-grandfather. A first cousin has ADHD, a first cousin once removed had major depressive disorder and committed suicide, another first cousin once removed had ADD. **Family 6:** This 6 year-old Hispanic boy has been diagnosed with autism spectrum disorder, mild mental retardation and anxiety disorder. His parents were unavailable for genetic testing. Family history was only significant for a maternal grandfather with epilepsy. **Family 7:** This boy of Vietnamese descent presented with global developmental delay and muscular hypotonia. There is no family history of neuro-psychiatric disease. **Family 8:** The 8-year-old index patient presented for evaluation of moderate mental retardation. Her mother as well as a maternal great-aunt have a history of depression. The maternal grandfather, maternal great-grandfather, and maternal great-uncle are alcoholics. These individuals are unavailable for genetic testing. **Family 9:** The 9-year-old propositus has autism spectrum disorder and mild mental retardation. His father, paternal grandmother, and two paternal aunts (the latter do not carry the microduplication of *CHRNA7*) have a history of major depressive disorder. **Family 10:** This 10-year old boy has been diagnosed with autism spectrum disorder, moderate mental retardation, and disruptive behavior disorder. His parents are currently unavailable for genetic testing. **Family 11:** The 12-year-old propositus had mild mental retardation, ADHD and bipolar disorder. His mother has ADHD, learning deficits, and major depressive disorder. A maternal great-aunt has bipolar disorder and anxiety disorder. The maternal great-grandmother has a history of depression, and the maternal great-grandfather is reported as physically violent. A maternal first cousin has ADHD, mental retardation, and epilepsy.

Supp. Table S1. Phenotypic features of 46 unrelated individuals with small microduplication of *CHRNA7*

Patient	Indication	Other CNVs Identified
1	Speech delay	
2	Feeding problem, FTT, Hypoglycemia	arr 5p15.2(9021335-9243037)x3.nuc ish 5p15.2(RP11-109L5x3)
3	GDD	
4	GDD	arr Xq25(123313165-123849841)x2.nuc ish Xq25(RP11-107O17x2)
5	Absent speech, GDD	arr 4q22.3(RP11-369l16)x1.ish del(4)(q22.3q22.3)(RP11-369l16dim)
6	Encephalopathy NOS	
7	GDD, Muscle weekness	arr 8q24.13q24.21(127185755-128672802)x1.ish del(8)(q24.13q24.13)(RP11-248A1-)
8	Encephalopathy	
9	Autism, speech disorder	
10	Microcephalus, GDD, Micropennis	
11	Mental retardation	arr 6q27(168458422-168622241)x3.nuc ish 6q27(RP11-673P11x3)
12	Mild DD/MR	
13	Moderate DD/MR	arr 17q12(33025190 - 33278963)x3.nuc ish 17q12(RP11-87D17x3)
15	Encephalopathy, Autism, GDD	
17	GDD	
18	Psychiatric diagnosis	
20	Autism	
21	ADHA, Dysmorphic features	
23	Mild DD/MR	
24	Conditions due to autosomal anomalies	
25	Moderate DD/MR, DF	arr 3q22.3(139610132-139871789)x3.nuc ish 3q22.3(RP11-946N8x3)
27	Down Syndrome, MCA	arr 8p23.3(305404-454943)x3.nuc ish 8p23.3(RP11-91J19x3)pat
28	GDD	
31	GDD	arr 18p11.31p11.23(6932021-8064261)x3.nuc ish 18p11.31(RP11-781P6x3)
34	Microcephaly	
37	GDD	arr 22q13.33(49484191-49525470)x1.ish del(22)(q13.33q13.33)(n85a3-)
38	Autistic Spectrum	arr 17q25.3(78459755-78586290)x3.nuc ish 17q25.3(RP11-629P20x3)
39	Mild GDD/MR	
42	Child with chromosome abnormality	
43	Dysmorphic features	arr 5q21.2q21.3(103818165-104883348)x3.nuc ish 5q21.2(RP11-6N13x3)
44	Multiple congenital anomalies, Pierre Robin Seq.	
46	FMHX of chromsome abnormality	
48	GDD	
49	DF, FTT, CMA	arr 1q21.1(145085612-145858878)x1.ish del(1)(q21.1q21.1)(RP11-337C18-)
51	Autism, GDD	arr 1q43(236497263 - 236637233)x3.nuc ish 1q43(RP11-136B18x3)
52	GDD, Dysmorphic features, ADHD	
53	Seizures	
54	Multiple congenital anomalies	
55	Short stature, Speech delay, DF	arr 22q11.21(17447366-19779911)x1.ish del(22)(q11.21q11.21)(D22S75-)
58	Limb anomaly, Radial ray defect	
59	Multiple congenital anomalies	
60	Encephalopathy	
62	Hydrocephalus	
63	Speech delay	
64	Moderate DD	
68	Abnormal ultrasound: hydrocephalus	

Supp. Table S2. DNA sequences of the MLPA probes used for verification of the identified small microduplications

Oligo Name	Sequence 5' to 3'	Product Size bp
CHRNA7 Exon 2 LS	**GGGTTCCCTAAGGGTTGGA**TGCAAGGCGAGTTCCAGAGGAAGCTTTAC	100
CHRNA7 Exon 2 RS	AAGGAGCTGGTCAAGAACTACAATCCCTTT**CTAGATTGGATCTTGCTGGCAC**	
CHRNA7 Exon 4 LS	**GGGTTCCCTAAGGGTTGGA**GTCAGAATATCCAGGGGTGAAGACTGTTCGT	104
CHRNA7 Exon 4 RS	TTCCCAGATGGCCAGATTTGGAAACCAGACAT**CTAGATTGGATCTTGCTGGCAC**	
CHRNA7/FAM Exon 5 LS	**GGGTTCCCTAAGGGTTGGA**GATGAGCGCTTTGACGCCACATTCCACACTAACGTG	114
CHRNA7/FAM Exon 5 RS	TTGGTGAATTCTTCTGGGCATTGCCAGTACCTGCCT**CTAGATTGGATCTTGCTGGCAC**	
CHRNA7/FAM Exon 10 LS	**GGGTTCCCTAAGGGTTGGA**GTGCTAATCCAGGACAGCATTACACGCCACAACTCCAG	118
CHRNA7/FAM Exon 10 RS	TGTTCCCTTCTGGCTGTCAGTCGTGTTGCTTACGGTTT**CTAGATTGGATCTTGCTGGCAC**	
OTUD7A Exon 9 LS	**GGGTTCCCTAAGGGTTGGA**TCCACGTTTTTGTCCTAGCCCATATATTAAGAAGGCCCAT	122
OTUD7A Exon 9 RS	CGTTGTTGTGGCAGATACAATGTTAAGAGACTCAGGTGGA**TCTAGATTGGATCTTGCTGGCAC**	
KLF13 Exon 2 LS	**GGGTTCCCTAAGGGTTGGA**TTCTCCGTGTCCCAGCAGAAGGCATGCAGGACCCTGTCACTACTAT	134
KLF13 Exon 2 RS	ACCTGGGCCTCTGATGGGGAATTCTGGTCTTCTAAAAAGATGTTAG**TCTAGATTGGATCTTGCTGGCAC**	
TRPM1 Exon 1 LS	**GGGTTCCCTAAGGGTTGGA**TCACTGCTCCATCTCATGGTGAAAGATTGGCAGCTGGAACTCCCCAAG	138
TRPM1 Exon 1 RS	CTCTTAATATCTGTGCATGGAGGCCTCCAGAACTTTGAGATGCAGCCC**TCTAGATTGGATCTTGCTGGCAC**	
MTMR10 Exon 14 LS	**GGGTTCCCTAAGGGTTGGA**GCTTCTCTTGTTCAAGTGATGCTGGATCCCTATTTTAGGACAATTACTGG	142
MTMR10 Exon 14 RS	ATTTCAGAGTCTGATACAGAAGGAGTGGGTCATGGCAGGATATCAGTTTC**TCTAGATTGGATCTTGCTGGCAC**	
MTMR15 Exon 2 LS	**GGGTTCCCTAAGGGTTGGA**TCTGCAGGATGACAGTTGCTTAAACAATGATATCCCTCACAGCATTCCTTTGGAG	152
MTMR15 Exon 2 RS	CAGGGGTCAAGCTGCAATGGTCCTGGTCAAACAACCGGTCATCCTTACTACCTTC**TCTAGATTGGATCTTGCTGGCAC**	
ARHGAP11B Exon 1 LS	**GGGTTCCCTAAGGGTTGGA**GAGTTATCGACGTATCCGGAATGTGGGATCAGAGGCTGGTGAAGTTGGCCCTGTTGC	156
ARHGAP11B Exon 1 RS	AGCATCTGCGGGCCTTCTATGGTATTAAGGTGAAGGGTGTCCGTGGGCAGTGCGATC**TCTAGATTGGATCTTGCTGGCAC**	
TJP1 Exon 12 LS	**GGGTTCCCTAAGGGTTGGA**TATTACGCCCGTGCCTTATCCGGAGAGGGAGGTGTTCCGTGTTGTGGATACCTTGTACA	160
TJP1 Exon 12 RS	ATGGAAAACTGGGCTCTTGGCTTGCTATTCGATGAATGACGCGACAGGAAGAACTTGAC**TCTAGATTGGATCTTGCTGGCAC**	
NDNL2 Exon 1 LS	**GGGTTCCCTAAGGGTTGGA**TCGGTGAGACGTGGGAGGCGAAAATTGGCGGAAGATTCCGATCAAGCGGGCCGACATACTG	164
NDNL2 Exon 1 RS	AAGCACGTCATCGGGGACTACAAGGACATCTAACGTCCGGATGCTGAAGTGATGGCAGAGC**TCTAGATTGGATCTTGCTGGCAC**	
APBA2 Exon 14 LS	**GGGTTCCCTAAGGGTTGGA**GAGCGGAAAGAGCATTATTCAGCGCCCGTTCCGGCAGGCTTTTTTCCAGACTCTAGGGTTTTC	168
APBA2 Exon 14 RS	CAATGTGACTAATGACCACACCTGCCTCTCCTGACCGTGTGGCTTACCTGACCGCCGGTATCG**TCTAGATTGGATCTTGCTGGCAC**	

Supp. Table S3. Long-range PCR primers used to map the NAHR sites

Patient	NAHR site	Initial PCR amplification and DNA sequencing	DNA sequencing across the NAHR breakpoint
3,23,54	1	5`GCAGTGAAGAGGGTAGTGAATGCTTTTAAC 5`ATTCTCTCTCTCTTCTCCCACTACCCTCAC	5`AAAGAGGCTTCTCACCCAGTTCAAATTGTTAC
38	1	5`GCAGTGAAGAGGGTAGTGAATGCTTTTAAC 5`ATTCTCTCTCTCTTCTCCCACTACCCTCAC	5`AAAGAGGCTTCTCACCCAGTTCAAATTGTTAC 5`GAGTCAGAGCCATGAAGATCCCATATTTTCTT
55	2	5`CTCTGACTTCTGAGATTCTGGTAGAGAGGTTC 5`GTGGTGACCAGTGACTCTATTTGTCGTATTC	5`AGTACTAGTCATGTCCCCTACTTGCCTATGGT
29	3	5`CTCTGACTTCTGAGATTCTGGTAGAGAGGTTC 5`GTGGTGACCAGTGACTCTATTTGTCGTATTC	5`CTTCTACTTGCTTTCAATTGCCTAAGCACAAC
Del4	4	5`GGTGACCAGTGACTCTGTATTTGTCGTATTC 5`GTAAAGATCTGGAAGGCTGAAGTGCTTCTC	5`CTTGCAAAACTTACCTGTTCTTCAAGTCAGTC
29,55	5	5`CTCTGACTTCTGAGATTCTGGTAGAGAGGTTC 5`GTGGTGACCAGTGACTCTATTTGTCGTATTC	5`AGAAACTCACATGAAGTTGCTGGTTAAGTGAC
13,29,55	6	5`CTCTGACTTCTGAGATTCTGGTAGAGAGGTTC 5`GTGGTGACCAGTGACTCTATTTGTCGTATTC	5`AATTATACTGTACTCCTGGATGGGGAAGCTGA 5`GCTCTACATTTAGGTTCAAAACCCATCTGGAA
8,15,31,37,60	6	5`CTCTGACTTCTGAGATTCTGGTAGAGAGGTTC 5`GTGGTGACCAGTGACTCTATTTGTCGTATTC	5`AGAATTAAAAGGGAGAACAGCCTTAGGAGAC
46	6	5`CTCTGACTTCTGAGATTCTGGTAGAGAGGTTC 5`GTGGTGACCAGTGACTCTATTTGTCGTATTC	5`AGAATTAAAAGGGAGAACAGCCTTAGGAGAC