Copy Number Variation Is An Important Contributor to the Genetic Causality of Inherited Retinal Degenerations

Short title: Copy Number Variation in Inherited Retinal Degenerations

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Supplementary information includes three tables, two figures and additional references.

Table S1. PCR primers (Primers in bold were used for amplification through the breakpoint. Sequences of the reference primers were taken from[1])

	Forward	Reverse
Reference primers		
GPR15_qPCR	GGTCCCTGGTGGCCTTAATT	TTGCTGGTAATGGGCACACA
ZNF80_qPCR	CTGTGACCTGCAGCTCATCCT	TAAGTTCTCTGACGTTGACTGATGTG
OGI-086 family		
OSKAR_ex4_qPCR	CAGCTTCATACCACCCTAAG	TTGAAAAGTCCAAATCTCCAAG
OSKAR_ex3_qPCR	CATTATAGGTGAGTACTGAAGAC	CTTGTTCTAGGTCATATGGTCAC
PRPF31_ex2_qPCR	GCTCTTAGCTGATCTCGAAG	GAAAGATCCAGCTGTGTCTC
PRPF31_ex8_qPCR	TGACCAACCTCTCCAAGATG	ATGTCACTGTGGTAGATGTAG
PRPF31_ex10_qPCR	ACGAACTGAAGGATGAGATC	CTTCTTCCGCTGTCCATC
PRPF31_ex14_qPCR	CAGAGAAGAAGGTGGCTGAG	AGTCATTCAGGTGGACATAAG
PRPF31_100bp_downstream_qPCR	CCCGTTACTTTCTCGTCATG	GTTGGCAGCCACATCATTTG
PRPF31_2K_downstream_qPCR	GAGGTTAAGGAAGAGCAACTC	**CTTGTAGGTCAGGTGACTAG**
PRPF31_6K_downstream_qPCR	CTAAACTTGACGGACGACTTC	GTCGTGCTGATTGGATGTATC
CNOT3_ex2_qPCR	TCTCCAATCTCTCCTAGCAG	GAAGTCAGTCTAGTACCTTG
OSKAR_intron3	**GACAGAGAGAAACTGGTCTC**	
OGI-014 family		
EYS_ex15_6K_upstream_qPCR	TGGACAAGTCACAGTATATGAG	GTATAAGAAGTACAGCACTGAGT
EYS_ex15_3K_upstream_qPCR	AACTTGGAAGAGAACTCCATTTC	CAGTGTACAAGAGTCAGTCAC
EYS_ex15_2K_upstream_qPCR	GGAACAGTTATTTTAAATTACTGGAATC	TTATTCATCAGTATCTTACTTGATTCA
EYS_ex15_1K_upstream_qPCR	CTAAGATGCGTTCTGTAATCTC	GATAATGCCAGCCCAGTTTC
EYS_ex15_qPCR	TTCTCTTAGAGCTACCAGTG	GGTGGAATTGTTCTTGCAAG
EYS_ex16_qPCR	TGTGAGTGTACATCTGGATG	GATGGTAGATTCATGACAAAG
EYS_ex17_qPCR	CATACTCTTTGCAGAATTTGAAG	GTTGACCATATCTTCACAGTC
EYS_ex18_qPCR	AAGGTGTATTTGCAGACCTG	GTTTGTCAGATCCACACATG
EYS_ex18_9.2K_downstream_qPCR	ATTACAATAACAGTGGCTAGTG	TCACAATATGCTTGTTGGTAATG
EYS_ex18_9.6K_downstream_qPCR	GAAGTGTGGTTCATGAATGCAG	CTGATAAGGACTTTTAAGCCTATG
EYS_ex18_12.7K_qPCR	TTATGGGTAGGTGTCAGAATC	TTTGTCATGATGAAGATGTGG
OGI-046 family		
ZAP70_qPCR	TGGACACGAGCGTGTATGAG	GTTCAATGTCAGCTATGAGGAG
SNRNP200_ex21_qPCR	TCTATGGCATCTCTCATGATG	GATTGTTCTTGTCCAGCATCAG
SNRNP200_ex22_qPCR	GTGCAGACTTACAACCAGCTGC	CTCTCTCACTGTGATGTTCTTG
SNRNP200_ex23_qPCR	TTGAGGAACCCAGTGCTAAG	CAAATTCAAGGTTCATCTTTTAGAAG
SNRNP200_ex25_qPCR	GAATGCTGCTTCTTTGCTTAG	GTTCAGGGTCTTGTCTGTAAG
SNRNP200_ex45_qPCR	TCCATGCTCATCTTGATTTCTG	GTCACTCATGAAGTACAGAGT
ANKDR36_ex41+100bp_qPCR	GCTGCACGTTCTGATTCACC	TGCTCTCCATGTTTCTTCCTCC
FAHD2B_ex8_qPCR	ATGTGTCTGACGGAAGGGCT	GCCATCACACCACCTTGTTG
GPAT2_ex1_qPCR	GGCGGGAATGAGTCCTTGTG	GAGCTACCCCAAGATGTGCG
ADRA2B_qPCR	TATCGGCCTTCCCTTGGAGA	CTCGGTGCCCTTCCAAATCT
OGI-036 family		
OPN1LW_CpG38_2K_upstream	**TAATTACAAAGGATTTGCAGGGAACAAG**	AATGGAGAAATAGAGAAAGGGCAAGAG
OPN1LW_CpG38_1K_upstream	TCAAATCATCAGATCCAAGACTCTAAGACA	AAAGCTTTCTACTGCCTTTGAACAGAAAAC
OPN1LW_CpG38	CGACCAGGATCCACCCTTTC	GCGGAAGGAGAGAGACATAATGG

OPN1LW_LCRcore	GCCCCCACAGGTGCTGAGTGACT	AGAGTGGAGGTGGCAGAGGTGGGAG
OPN1LW_ex5		**CAGACGCAGTACGCAAAGAT**

Table S2. Computationally predicted NAHR-prone regions in the genome

Chromosome	Start	End	IRD gene	Comments
chr1	88,000	712,554		
chr1	1,567,836	1,683,632	*GNB1*	33.1kb away from NAHR, CNVs never described before
chr1	12,840,257	13,774,009		
chr1	16,825,367	21,784,068	*EMC1, PLA2G5*	direct overlap with NAHR, CNVs never described before
chr1	25,594,515	25,751,819		
chr1	39,975,198	40,242,350		
chr1	47,304,216	47,622,817		
chr1	103,785,265	104,003,638		
chr1	104,161,927	104,317,467		
chr1	108,764,242	109,015,286		
chr1	121,361,171	121,472,478		
chr1	142,542,267	143,544,525		
chr1	143,644,525	149,847,929		
chr1	161,479,597	161,646,894		
chr1	196,711,704	196,920,352		
chr1	222,650,092	228,173,643		
chr1	248,584,239	248,834,181		
chr2	77,901,296	92,254,230		
chr2	96,080,043	98,250,348	*SNRNP200, CNNM4*	direct overlap with NAHR, CNVs in *SNRNP200* never described before and in *CNNM4* only affecting certain exons
chr2	100,697,051	113,207,451	*NPHP1, MERTK*	direct overlap with NAHR, CNVs affecting the entire gene (*NPHP1*) or certain exons (*MERTK*) observed previously
chr2	130,735,169	132,308,920		
chr2	243,088,899	243,189,373		
chr3	123,675,719	125,715,090		
chr3	195,349,462	197,394,388	*PCYT1A*	direct overlap with NAHR, CNVs never described before
chr4	8,943,507	9,552,539		
chr4	49,154,264	49,637,650		
chr4	69,678,647	69,889,161		
chr4	70,035,680	70,269,147		
chr4	75,282,464	75,493,261		
chr4	119,521,346	120,361,492		
chr4	144,706,829	145,070,347		
chr5	235,806	1,617,110		
chr5	17,497,010	17,634,140		
chr5	21,504,597	29,456,424		
chr5	68,829,716	70,660,316		
chr5	98,726,330	99,736,930		
chr5	175,329,459	177,482,249		
chr6	26,702,386	26,798,341		
chr6	31,948,308	31,999,999	*STK19*	direct overlap with NAHR, CNVs affecting the entire gene observed previously
chr6	52,610,640	52,680,222		
chr6	57,686,350	58,726,206		
chr6	167,579,270	167,806,139		
chr7	5,016,599	5,778,292		
chr7	29,692,579	35,231,074	*RP9, BBS9*	direct overlap with NAHR, CNVs in *RP9* never described before and in *BBS9* only affecting certain exons
chr7	35,953,035	56,496,499		
chr7	57,670,560	57,914,373		
chr7	61,056,562	61,845,697		
chr7	62,678,540	62,985,366		
chr7	64,471,586	65,367,315		

chr7	65,894,273	76,691,789	*KCTD7*	direct overlap with NAHR, CNVs only affecting certain exons observed before
chr7	101,982,123	102,319,899		
chr7	143,218,861	143,571,789		
chr7	143,884,041	144,074,376		
chr7	149,586,782	153,864,361	*NUB1*	direct overlap with NAHR, CNVs never described before
chr8	2,180,177	2,343,982		
chr8	7,005,690	7,999,583		
chr8	11,895,289	12,334,342		
chr8	12,408,472	12,525,492		
chr8	86,552,568	86,841,605		
chr8	142,754,395	142,970,306		
chr8	145,187,380	145,501,700		
chr9	33,382,122	47,317,679		
chr9	65,817,023	71,031,684		
chr9	85,042,171	94,872,062		
chr9	97,069,068	99,789,772		
chr10	4,968,124	5,074,055		
chr10	14,974,843	15,068,904		
chr10	17,777,711	18,221,580		
chr10	43,189,721	45,644,459		
chr10	46,171,743	52,544,109	*RBP3, ERCC6*	direct overlap with NAHR, CNVs in *RBP3* never described before and entire gene CNVs in *ERCC6* observed previously
chr10	81,260,743	89,260,363	*CDHR1, RGR*	direct overlap with NAHR, CNVs never described before
chr10	135,236,150	135,394,059		
chr11	3,268,109	3,359,713		
chr11	4,252,196	4,363,052		
chr11	48,416,917	51,552,637		
chr11	55,046,069	55,661,495		
chr11	58,803,450	58,881,318		
chr11	67,477,730	71,515,825	*LRP5*	direct overlap with NAHR, CNVs affecting certain exons observed before
chr11	89,475,576	89,830,683		
chr12	9,436,203	9,600,866		
chr12	63,923,418	64,146,247		
chr12	131,766,776	132,169,194		
chr13	19,773,434	25,555,912	*IFT88*	direct overlap with NAHR, CNVs affecting the entire gene observed previously
chr13	52,771,866	53,187,379		
chr13	64,290,924	64,418,388		
chr14	19,361,502	20,194,548		
chr14	24,421,111	24,503,512	*NRL*	46kb away from NAHR, CNVs never described before
chr14	74,000,098	74,052,473		
chr14	106,044,744	106,244,200		
chr15	20,198,575	32,925,115	*OCA2, TRPM1*	direct overlap with NAHR, CNVs affecting the entire gene observed previously in both cases
chr15	34,671,002	34,875,898		
chr15	43,851,135	44,041,710		
chr15	45,109,634	45,375,390		
chr15	72,911,806	78,251,250	*BBS4*	direct overlap with NAHR, CNVs affecting certain exons observed before
chr15	78,259,695	79,078,694	*CIB2*	direct overlap with NAHR, CNVs affecting certain exons observed before
chr15	82,483,003	85,815,511		
chr15	100,319,313	102,334,597		
chr16	2,584,142	2,741,054		
chr16	12,018,586	30,346,868	*ABCC6, CLN3*	direct overlap with NAHR, CNVs affecting the entire gene (*ABCC6*) or certain

				exons (*CLN3*) observed previously
chr16	31,961,153	33,864,470		
chr16	69,977,498	74,590,161	*DHX38*	direct overlap with NAHR, CNVs never described before
chr17	2,954,154	3,156,719		
chr17	13,923,279	22,075,527		
chr17	28,927,470	30,415,970		
chr17	34,481,812	45,671,436	*GPR179, GRN*	direct overlap with NAHR, CNVs in *GPR179* never described before and entire gene CNVs in *GRN* observed previously
chr17	57,650,241	58,079,963		
chr17	58,083,345	60,375,823	*CA4*	direct overlap with NAHR, CNVs affecting the entire gene observed previously but in a different phenotype
chr17	77,495,191	77,630,507		
chr18	10,604,201	12,231,380		
chr19	12,496,799	12,555,157		
chr19	20,504,255	20,595,412		
chr19	22,559,977	22,862,402		
chr19	36,758,541	37,796,694		
chr19	41,336,556	41,393,307		
chr19	43,233,122	43,801,771		
chr19	43,840,402	43,901,918		
chr19	48,406,743	51,126,682	*CRX*	60kb away from NAHR, CNVs affecting certain exons observed before
chr20	25,733,092	26,084,413		
chr20	46,453,805	46,534,975		
chr21	9,645,548	10,203,948		
chr21	15,346,934	15,441,979		
chr22	17,005,667	25,080,013		
chr22	25,622,856	26,013,117		
chr22	42,902,112	42,978,456		
chrX	1,035,193	1,210,363		
chrX	3,734,603	3,856,330		
chrX	36,986,405	37,454,830		
chrX	47,863,712	48,002,428		
chrX	48,100,846	52,837,913	*CACNA1F*	direct overlap with NAHR, CNVs affecting certain exons observed before
chrX	52,903,909	53,006,000		
chrX	55,479,962	55,546,105		
chrX	62,347,592	62,470,907		
chrX	70,899,842	71,025,014		
chrX	71,955,011	72,210,791		
chrX	101,452,530	101,744,479		
chrX	103,223,668	103,324,337		
chrX	119,172,167	119,332,013		
chrX	120,063,235	120,120,871		
chrX	134,250,050	134,390,361		
chrX	134,745,204	134,812,220		
chrX	134,846,411	134,971,858		
chrX	139,086,368	139,311,560		
chrX	140,077,191	140,789,063		
chrX	148,613,958	149,116,021		
chrX	151,847,040	151,958,439		
chrX	152,229,636	152,560,433		
chrX	153,444,157	153,519,082	*OPN1LW, OPN1MW*	adjacent and direct overlap with NAHR, CNVs affecting the entire gene observed previously
chrX	153,564,285	153,624,563		
chrX	153,783,899	153,877,056	*IKBKG*	direct overlap with NAHR, CNVs affecting the entire gene observed previously
chrX	154,566,001	154,734,211		
chrY	15,438	116,217		
chrY	6,107,831	9,752,225		

chrY	16,093,531	16,172,355		
chrY	18,271,431	18,537,677		
chrY	19,567,683	28,457,769		
chrY	58,819,361	58,917,656		

Table S3. Patients' phenotypes

Patient	Age	Visual acuity		Visual fields (I-4e/V-4e)		Scotopic ERG (μV)		30Hz ERG (μV)		Photopic ERG implicit time (ms)		Additional features
		OD	OS	OD	OS	OD	OS	OD	OS	OD	OS	
OGI-086-213	18	20/40	20/30	10°/60°	10°/50°	ND	ND	0.36	0.56	35	37	Anterior polar cataracts, nyctalopia and photophobia since early childhood, salt and pepper peripheral retinopathy fundus appearance
OGI-036-091	10	20/200	20/200	110°/full	90°/full	289	295	0.88	0.74	50	47	Abnormal color vision, nystagmus, fine pigment granularity in the maculas.
OGI-036-336	17	20/125	20/250	112°/full	110°/full	244	201	0.48	0.34	39	40	Abnormal color vision, nystagmus, fine pigment granularity in the maculas.
OGI-046-116	11	20/25	20/25	constricted	constricted	NA	NA	NA	NA	NA	NA	Elevated dark adaptation thresholds (2-3 log units), reported difficulties of night vision, bone-spicule pigmentation in retinal peripheries, thinning photoreceptor layers in the periphery as seen by OCT, normal color vision. No extra-ocular symptoms noted.
OGI-014-038*	46	LP	20/300	minimal crescent in temporal periphery	minimal crescent in temporal periphery	ND	ND	ND	ND	ND	ND	Absent color vision, nyctalopia at 15 years
OGI-023-057*	11	20/125	20/160	NA	NA	Normal	Normal	Absent	Absent	Not applicable	Not applicable	Nystagmus in infancy, exotropia, photophobia and abnormal color vision; amelogenesis imperfecta

Scotopic ERG: white stimulus 0.5Hz (normal range: 350-700 μV), 30Hz ERG: white stimulus (normal range: 50-125 μV), Implicit time (normal range: 25-32 ms). Color vision measured on Farnsworth D15 and /or Ishihara tests. *These patients were seen at CHOP. An ISCEV-standard ERG was performed at CHOP in patient OGI-023-057. Abbreviations: NA: not available, ND: not detectable.

Supplementary Materials

Table S4. Rare variants found from WES

Gene	Refseq ID	gDNA change	cDNA change	Effect	dbSNP	1000G MAF	ExAC MAF	OGI	GERP	Sift	Pph2	Ret Exp	Cosegregation					
OGI-014													**OGI-014-038**	**OGI-014-039**	**OGI-014-154**	**OGI-014-289**		
PNPLA4	NM_004650	chrX:g.7870085G>A	c.575C>T	p.P192L	rs148618718	0.00%	0.02%	2	3.94	D	D	25.2	hom		het			
XDH	NM_000379	chr2:g.31557740delT	c.*1084delA	3' UTR	NA	0.00%	0.00%	2	-0.234	-	-	6.5	het		het			
XDH	NM_000379	chr2:g.31564244A>G	c.3536T>C	p.I1179T	rs139515054	0.04%	0.37%	11	5.48	D	D	28.0	het	het		het		
CCDC66	NM_001141947	chr3:g.56600608A>G	c.545-14A>G	Extended splice site	rs78488477	0.14%	0.33%	8	4.42	-	-	-	het		het			
CCDC66	NM_001141947	chr3:g.56655621A>G	c.2822A>G	p.E941G	rs144848139	0.06%	0.19%	12	5.37	D	D	21.3	het	het				
IYD	NM_001164694	chr6:g.150719248G>A	c.857G>A	p.G286D	rs202223369	0.02%	0.01%	3	-3.29	D	B	0.0	het		het	het		
IYD	NM_001164694	chr6:g.150721206G>A	c.*1933G>A	3' UTR	rs146165286	0.08%	0.00%	6	1.23	-	-	0.0	het	het				
STEAP2	NM_001040665	chr7:g.89856643A>G	c.851A>G	p.Y284C	rs138124501	0.14%	0.45%	13	6.04	D	D	6.0	het		het			
STEAP2	NM_001040665	chr7:g.89863143A>G	c.*1205A>G	3' UTR	NA	0.02%	0.00%	2	0.116	-	-	4.1	het	het				
KRT84	NM_033045	chr12:g.52774244G>A	c.1327C>T	p.R443W	rs138689455	0.00%	0.01%	2	0.34	D	D	0.0	het		het			
KRT84	NM_033045	chr12:g.52779006A>C	c.364T>G	p.F122V	rs144471272	0.04%	0.16%	6	5.05	D	D	0.1	het	het		het		
STARD9	NM_020759	chr15:g.42979360_42979365delAGCACA	c.5584_5589del	p.S1862_T1863del	NA	0.06%	0.14%	3	-7.43	-	-	3.2	het	het		het		
STARD9	NM_020759	chr15:g.42982579G>C	c.8803G>C	p.E2935Q	rs201158158	0.00%	0.00%	2	3.82	T	-	3.2	het		het			
MYO1C	NM_001080779	chr17:g.1384184G>T	c.628-5C>A	Extended splice site	rs201919233	0.12%	0.15%	9	1.72	-	-	-	het	het				
MYO1C	NM_001080779	chr17:g.1387470C>T	c.203G>A	p.R68Q	NA	0.02%	0.01%	2	3.55	T	P	17.5	het		het			
OGI-036													**OGI-036-091**	**OGI-036-336**	**OGI-036-753**	**OGI-036-333**	**OGI-036-334**	**OGI-036-335**
GPM6B	NM_001001995	chrX:g.13790475A>G	c.*525T>C	3' UTR	rs189371743	0.32%	0.00%	23	-6.56	-	-	43.7	hom	hom	hom	het	-	-
DMD	NM_004007	chrX:g.31792064T>C	c.7173+13A>G	Extended splice site	rs72466585	0.32%	0.39%	21	-2.82	-	-	-	hom	hom	hom	het	-	-
ZNF449	NM_152695	chrX:g.134496662A>G	c.*1661A>G	3' UTR	NA	0.00%	0.00%	5	3.32	-	-	1.8	hom	hom	hom	het	-	-
MMGT1	NM_173470	chrX:g.135044584A>G	c.*2599T>C	3' UTR	NA	0.00%	0.00%	5	3.56	-	-	11.4	hom	hom	hom	het	-	-
OGI-046													**OGI-046-116**		**OGI-046-114**		**OGI-046-115**	

Supplementary Materials

CHDC2	NM_173695	chrX:g.36091382A>G	c.317A>G	p.Y106C	rs146638559	0.00%	0.00%	2	-7.57	T	B	0.3	hom		het
ZBTB33	NM_006777	chrX:g.119389143C>T	c.1873C>T	p.P625S	rs79151935	0.00%	0.04%	3	4.96	T	D	6.5	hom		het
PNMA3	NM_013364.4	chrX:g.152226562C>T	c.1150C>T	p.R384W	rs144738062	0.00%	0.02%	2	-0.0351	D	P	1.1	hom		het
TAZ	NM_000116	chrX:g.153648024C>T	c.542-20C>T	Extended splice site	rs373841640	0.00%	0.04%	2	-1.66	-	-	8.3	hom		het
SNRNP200	NM_014014	chr2:g.96954816G>T	c.3133C>A	p.P1045T	NA	0.00%	0.00%	2	5.5	D	NA	175.5	hom	het	
ABCA12	NM_173076	chr2:g.215914490A>G	c.553T>C	p.C185R	NA	0.00%	0.00%	2	6.05	D	D	4.1	hom	het	
CLDN1	NM_021101	chr3:g.190030679C>T	c.370G>A	p.A124T	rs140846629	0.14%	0.38%	1	2.79	D	B	76.9	hom		
IFT52	NM_016004	chr20:g.42265804G>A	c.1031G>A	p.R344Q	rs145627647	0.06%	0.06%	6	5.27	T	P	24.4	hom	het	het
DGCR6L	NM_033257	chr22:g.20303706G>A	c.308C>T	p.A103V	NA	0.00%	0.02%	1	1.98	T	B	40.5	hom		
DIEXF	NM_014388	chr1:g.210024715G>A	c.2194G>A	p.V732M	rs61742373	0.12%	0.06%	3	5.95	D	D	1.2	het		het
DIEXF	NM_014388	chr1:g.210030577T>C	c.*5785T>C	3' UTR	NA	0.00%	0.00%	2	-0.145	-	-	1.2	het	het	
PLEC	NM_201384	chr8:g.144996761C>T	c.7336G>A	p.E2446K	NA	0.00%	0.00%	2	4.56	D	P	16.1	het	het	
PLEC	NM_201384	chr8:g.144999731C>T	c.4366G>A	p.V1456M	rs186848953	0.16%	0.48%	7	3.56	D	NA	16.1	het		het
SLC15A4	NM_145648.3	chr12:g.129278784T>G	c.1691A>C	p.Q564P	NA	0.00%	0.00%	2	5.27	T	B	32.9	het		het
SLC15A4	NM_145648.3	chr12:g.129299388G>A	c.774C>T	p.(=)	NA	0.02%	0.03%	2	-11.4	-	-	23.3	het	het	
CACNA1I	NM_021096	chr22:g.40058393A>T	c.3325A>T	p.M1109L	rs58021347	0.10%	0.28%	14	5.1	T	-	0.9	het	het	
CACNA1I	NM_021096	chr22:g.40082469G>A	c.*59G>A	3'UTR	NA	0.00%	0.00%	10	3.95	-	-	1.6	het		het
OGI-086													**OGI-086-213**	**OGI-086-215**	**OGI-086-214**	**OGI-086-635**
FAM9A	NM_174951	chrX:g.8763254_8763256delCTC	c.694_696del	p.E232del	NA	0.00%	0.44%	8	0	-	-	0.0	hom			het
AMELX	NM_182680	chrX:g.11316275A>G	c.144+11A>G	Extended splice site	rs200163085	0.34%	0.49%	18	-2.49	-	-	-	hom			het
SSX5	NM_021015	chrX:g.48054711T>A	c.69+15A>T	Extended splice site	rs199714668	0.00%	0.06%	6	-1.73	-	-	-	hom			het
PHKA1	NM_001122670	chrX:g.71856147T>C	c.1549A>G	p.I517V	NA	0.00%	0.00%	4	5.96	D	B	17.4	hom			het
BARX2	NM_003658.4	chr11:g.129306573G>A	c.188-73G>A	Extended splice site	NA	0.00%	0.00%	8	0.278	-	-	2.7	hom	het		het
PON3	NM_000940	chr7:g.94989379C>T	c.971G>A	p.G324D	rs139856535	0.16%	0.28%	10	4.7	D	D	0.8	het		het	

Supplementary Materials

PON3	NM_000940	chr7:g.95001590T>C	c.262A>G	p.M88V	rs78883915	0.04%	0.09%	14	3.67	D	B	2.2	het	het		het
PDHX	NM_001135024	chr11:g.34982064G>C	c.595G>C	p.E199Q	rs146445744	0.00%	0.04%	12	5.99	T	P	49.0	het	het		het
PDHX	NM_001135024	chr11:g.35016546T>G	c.1288T>G	p.F430V	rs147948716	0.16%	0.13%	7	6.04	T	P	14.9	het		het	

Abbreviations: dbSNP – Single Nucleotide Polymorphism database (http://www.ncbi.nlm.nih.gov/SNP/), MAF – minor allele frequency, 1000G – 1000 Genomes Project (http://www.1000genomes.org/), ExAC- Exome Aggregation Consortium (http://exac.broadinstitute.org/), OGI – Ocular Genomics Institute internal frequency database, Genomic Evolutionary Rate Profiling (GERP), Pph – Polyphen2, Ret Exp – retinal expression based on the study of [2], similar retinal expression was seen in Human Proteome Map [3].

Supplementary Materials

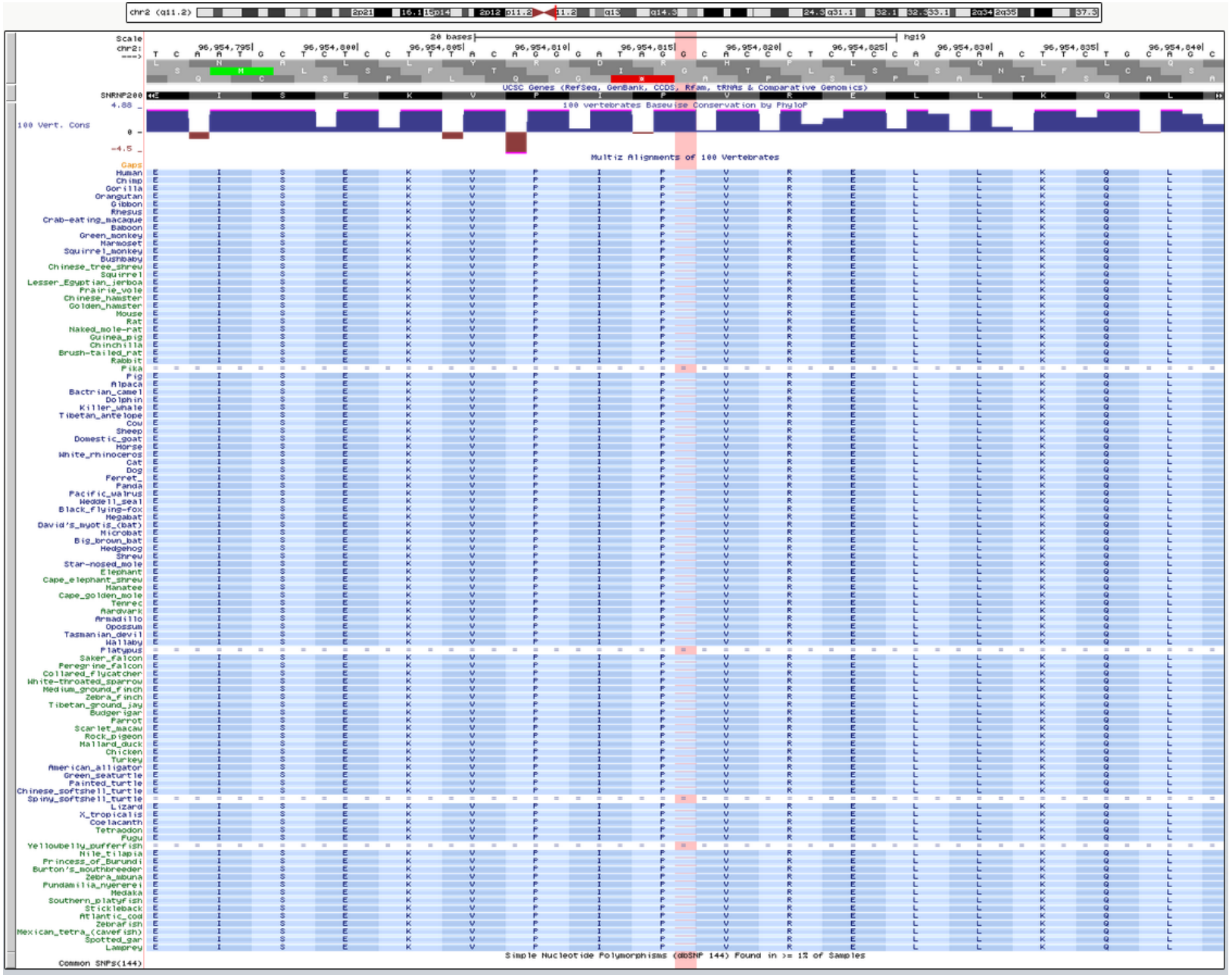

Figure S1. Conservation of the P1045 residue in *SNRNP200*

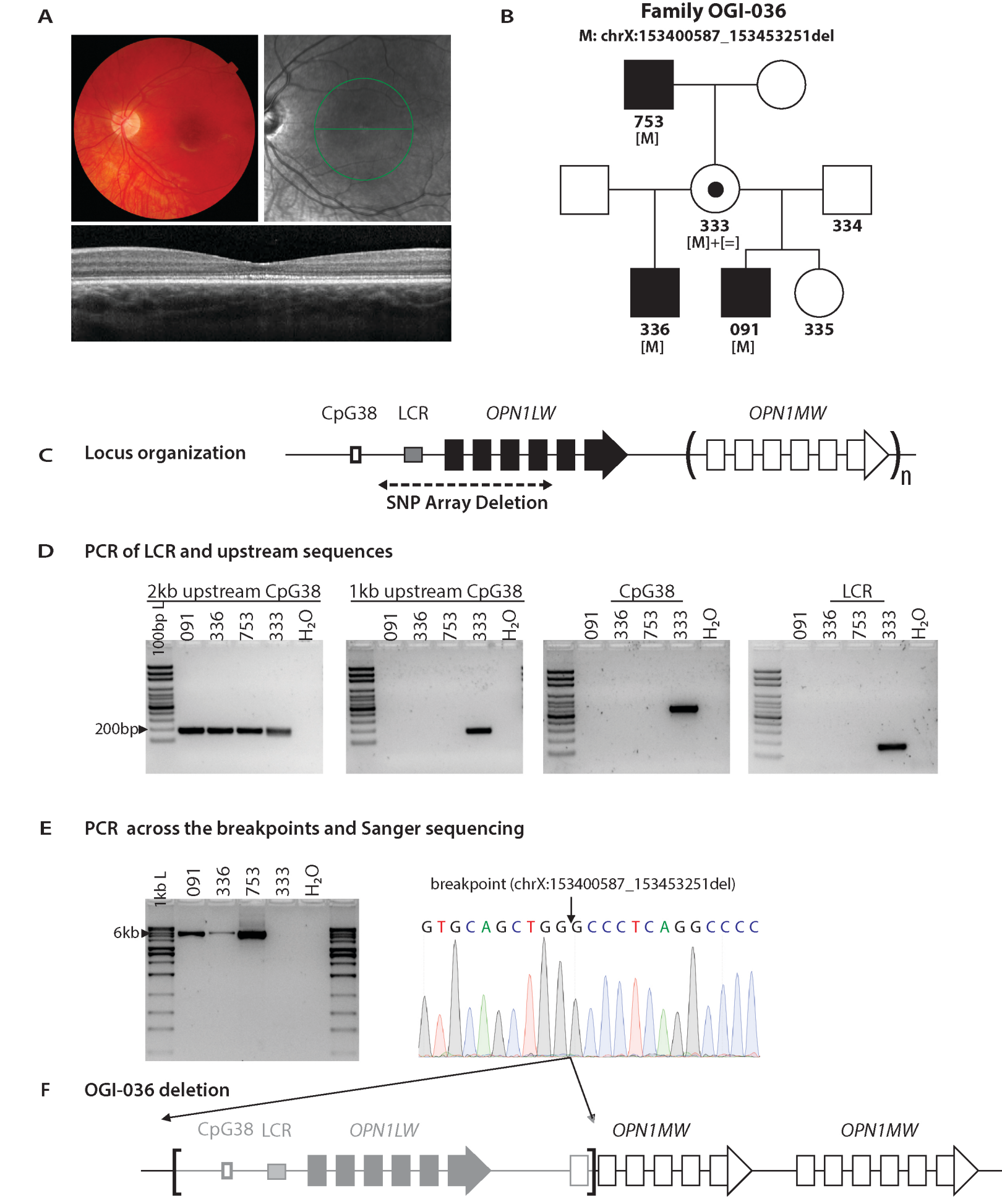
A
B
Family OGI-036
M: chrX:153400587_153453251del
753
[M]
333
[M]+[=]
334
336
[M]
091
[M]
335
C
Locus organization
CpG38
LCR
OPN1LW
OPN1MW
n
SNP Array Deletion
D
PCR of LCR and upstream sequences
2kb upstream CpG38
1kb upstream CpG38
CpG38
LCR
100bp L
091
336
753
333
H2O
200bp
E
PCR across the breakpoints and Sanger sequencing
1kb L
6kb
breakpoint (chrX:153400587_153453251del)
G T G C A G C T G G G C C C T C A G G C C C C
F
OGI-036 deletion
CpG38
LCR
OPN1LW
OPN1MW
OPN1MW

Figure S2. Deletion mapping in family OGI-036. A) Phenotype of patient OGI-036-091, represented by color fundus photograph of the left eye (top left), infrared fundus reference image (top right) and OCTcross-sectional scan (bottom). B) Pedigree of family OGI-036 with mutant allele segregation. C) Organization of the long wavelength (*OPN1LW*) and the medium wavelength (*OPN1LM*) opsin genomic region with locus control region (LCR) and a CpG island. The deletion detected by the Omni 2.5 SNP array is indicated by a dashed arrow. D) PCR amplification of selected regions upstream of the *OPN1LW* gene. E) PCR amplification across the breakpoints and Sanger sequencing electropherogram showing the precise position of the deletion. F) A map of the deleted region.

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