

# ***CNGB1*-related rod-cone dystrophy: a mutation review and update.**

**Nassisi et al.**

## **Supplemental Material**

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### **References**

**Table S1.** *In silico* analysis performed on the *CNGB1* variants included in the study. PhyloP range: -14.1;6.4. Grantham score range: 0;215. CNBD: cyclic nucleotide binding domain; CaMBD: Calmodulin binding domain

Genomic start position (hg19)	Exon/ Intron	cDNA (NM_001297.5)	Protein change (NP_001288.3)	Protein domain involved/putative functional consequence	rs#; gnomAD: frequency (allele count/total alleles/number of homozygous)	PhyloP	Grantham	Pathogenic prediction for missense changes			Effect on splicing prediction		
								SIFT (score)	Mutatio nTaster (prob)	PolyPhen 2 (score)	MaxEnt	NNSplice	SSF
58001027	IVS2	c.159+5G>A	p.?	Possible effect on splicing leading to a shorter/longer protein product or NMD	no rs#; gnomAD: absent	-	-	-	-	-	-92.20%	-95.70%	-14.90%
57998386	IVS3	c.217+5G>C	p.?	Possible effect on splicing leading to a shorter/longer protein product or NMD	rs527236060; gnomAD: 0.0046% (13/280826/0)	-	-	-	-	-	-70.10%	-51.70%	-14.70%
57998062	4	c.262C>T	p.(Gln88*)	Premature stop codon leading to a shorter protein product with only the N-terminus fragment or NMD	rs878853394; gnomAD: absent	-	-	-	Disease Causing (1)	-	-	-	-
57996944	5	c.315G>A	p.(Trp105*)	Premature stop codon leading to a shorter protein product with only the N-terminus fragment or NMD	rs1420628245; gnomAD: 0.0004% (1/248694/0)	-	-	-	Disease Causing (1)	-	-	-	-
57996913	5	c.346C>T	p.(Gln116*)	Premature stop codon leading to a shorter protein product with only the N-terminus fragment or NMD	rs367677784; gnomAD: 0.0004% (1/249010/0)	-	-	-	Disease Causing (1)	-	-	-	-

57996773	6	c.385del	p.(Leu129 Trpfs*148 )	Premature stop codon leading to a shorter protein product with only the N-terminus fragment or NMD	no rs#; gnomAD: absent	-	-	-	Disease Causing (1)	-	-	-	-
57996515	IVS6	c.413-1G>A	p.[= ; Cys139Alafs*138]#	Creation of a cryptic splice site downstream, leading to the loss of the first nucleotide of exon 7, hence to a frameshift	rs189234741; gnomAD: 0.0075% (21/280578/0)	-	-	-	-	-	-100.00%	-100.00%	-100.00%
57994756	8	c.522dup	p.(Lys175 Glufs*4)	Premature stop codon leading to a shorter protein product with only the N-terminus fragment or NMD	no rs#; gnomAD: 0.0004% (1/248226/0)	-	-	-	Disease Causing (1)	-	-	-	-
57994743	IVS8	c.534+1G>A	p.?	Possible effect on splicing leading to a shorter/longer protein product or NMD	rs200862689; gnomAD: 0.0036% (9/248004/0)	-	-	-	-	-	-100.00%	-100.00%	-100.00%
57993889	10	c.664C>T	p.(Gln222 *)	Premature stop codon leading to a shorter protein product with only the N-terminus fragment or NMD	rs570828500; gnomAD: 0.0005% (1/210288/0)	-	-	-	Disease Causing (1)	-	-	-	-
57992344	11	c.807G>C	p.(Gln269 His)	GARP Domain	no rs#; gnomAD: absent	0,69	24	Deleterious (0)	Polymorphism (0.997)	Probably Damaging (0.995)	-	-	-
57992319	11	c.832G>T	p.(Glu278 *)	Premature stop codon leading to a shorter protein product with only the N-terminus fragment or NMD	no rs#; gnomAD: absent	-	-	-	Disease Causing (1)	-	-	-	-
57993790	IVS10	c.761+2T>A	p.?	Possible effect on splicing leading to a	no rs#; gnomAD: absent	-	-	-	-	-	-100.00%	-100.00%	-100.00%

				shorter/longer protein product or NMD									
57984446	IVS12	c.875-2A>C	p.?	Possible effect on splicing leading to a shorter/longer protein product or NMD	no rs#; gnomAD: absent	-	-	-	-	-	-100.00%	-100.00%	-100.00%
57984428	IVS12	c.875-5_891del	p.?	Premature stop codon leading to a shorter protein product with only the N-terminus fragment or NMD	no rs#; gnomAD: absent	-	-	-	-	-	-100.00%	-100.00%	-100.00%
57984380	13	c.939G>A	p.(Trp313*)	Premature stop codon leading to a shorter protein product with only the N-terminus fragment or NMD	no rs#; gnomAD: absent	-	-	-	Disease Causing (1)	-	-	-	-
57984367	13	c.952C>T	p.(Gln318*)	Premature stop codon leading to a shorter protein product with only the N-terminus fragment or NMD	rs372504780; gnomAD: 0.0008% (2/249588/0)	-	-	-	Disease Causing (1)	-	-	-	-
57974234	IVS14	c.1122-9G>A	p.[=; Glu374Glu fs*7]†	Causes retention of 7 bp of intron 14 resulting in a frameshift with stop codon 7AA downstream of exon 15.	rs750225817; gnomAD: 0.0024% (5/208958/0)	-	-	-	-	-	-100.00%	-10.90%	-100.00%
57974160	15	c.1187G>A	p.(Arg396Gln)	Linker GARP-Channel domain	rs370327030; gnomAD: 0.0046% (10/216252/0)	-0,68	43	Tolerated (0.58)	Polymorphism (1)	Benign (0)	-	-	-
57973487	16	c.1219dup	p.(Glu407Glyfs*12)	Premature stop codon leading to a shorter protein product with only the N-terminus fragment or NMD	no rs#; gnomAD: absent	-	-	-	Disease Causing (1)	-	-	-	-

57973394	16	c.1312C>T	p.(Gln438*)	Premature stop codon leading to a shorter protein product with only the N-terminus fragment or NMD	rs776632878; gnomAD: 0.0008% (2/246622/0)	-	-	-	-	Disease Causing (1)	-	-	-	-
57973387	16	c.1319G>A	p.(Trp440*)	Premature stop codon leading to a shorter protein product with only the N-terminus fragment or NMD	no rs#; gnomAD: absent	-	-	-	-	Disease Causing (1)	-	-	-	-
57965773	17	c.1382C>T	p.(Thr461Met)	Linker GARP-Channel domain	rs147593839; gnomAD: 0.8955% (2513/280628/44)	3,35	81	Tolerated (0.13)	Polymorphism (0.888)	Probably Damaging (1)	-	-	-	-
57957231	18	c.1589C>G	p.(Pro530Arg)	Linker GARP-Channel domain	rs201553871; gnomAD: 0.0401% (117/280670/2)	0,85	103	Tolerated (0.17)	Disease causing (0.073)	Probably Damaging (0.998)	-	-	-	-
57957207	18	c.1613G>A	p.(Trp538*)	Premature stop codon leading to a shorter protein product with only the N-terminus fragment or NMD	rs1258900049; gnomAD: 0.0004% (1/249196/0)	-	-	-	-	Disease Causing (1)	-	-	-	-
57954451	IVS18	c.1644-3C>G	p.?	Possible effect on splicing leading to a shorter/longer protein product or NMD	no rs#; gnomAD: 0.0004% (1/247932/0)	-	-	-	-	-	-100.00%	-99.90%	-13.70%	-
57954363	19	c.1729del	p.(Glu577Serfs*6)	Premature stop codon leading to a shorter protein product with only the N-terminus fragment or NMD	no rs#; gnomAD: absent	-	-	-	-	Disease Causing (1)	-	-	-	-
57954286	IVS19	c.1801+5G>A	p.?	Possible effect on splicing leading to a shorter/longer protein product or NMD	rs375550800; gnomAD: 0.0025% (7/280852/0)	-	-	-	-	-	-100.00%	-98.50%	-16.40%	-

57953064	20	c.1896C>A	p.(Cys632*)	Premature stop codon leading to a shorter protein product with only the N-terminus fragment or NMD	rs774264204; gnomAD: 0.0004% (1/249562/0)	-	-	-	Disease Causing (1)	-	-	-	-
57953043	20	c.1917G>A	p.(Trp639*)	Premature stop codon leading to a shorter protein product with only the N-terminus fragment or NMD	rs183443649; gnomAD: 0.0004% (1/249570/0)	-	-	-	Disease Causing (1)	-	-	-	-
57953019	20	c.1941C>A	p.(Ser647Arg)	Linker GARP-Channel domain	rs1187092335; gnomAD: 0.0008% (2/249554/0)	-	-	Deleterious (0.01)	Disease Causing (1)	Probably Damaging (0,997)	-	-	-
57953001	IVS20	c.1957+2T>G	p.?	Possible effect on splicing leading to a shorter/longer protein product or NMD	rs755398007; gnomAD: 0.0012% (3/249502/0)	-	-	-	-	-	-100.00%	-100.00%	-100.00%
57951234	21	c.2093_2104dup	p.(Cys698_Ile701dup)	Longer protein product with possible effect on the overall structure of the protein	No rs#; gnomAD: absent	-	-	-	Disease Causing (1)	-	-	-	-
57951242	21	c.2096A>G	p.(Asp699Gly)	TD2	rs878853393; gnomAD: absent	3,27	94	Deleterious (0)	Disease Causing (1)	Probably Damaging (1)	-	-	-
57951166	IVS21	c.2166+6T>C	p.?	Possible effect on splicing leading to a shorter/longer protein product or NMD	rs771401261; gnomAD: 0.0032% (9/274684/0)	-	-	-	-	-	-48.6%	-62.7%	-7.8%
57950065	22	c.2185C>T	p.(Arg729*)	Premature stop codon leading to a shorter protein product with only the N-terminus fragment or NMD	no rs#; gnomAD: 0.0011% (3/280968/0)	-	-	-	Disease Causing (1)	-	-	-	-

57950040	22	c.2210G>A	p.(Arg737 His)	TD3	rs764107600; gnomAD: 0.0018% (5/280948/0)	4,81	29	Deleterious (0.03)	Disease Causing (1)	Probably Damaging (0.999)	-	-	-
57949241	IVS22	c.2218-2A>G	p.?	Possible effect on splicing leading to a shorter/longer protein product or NMD	no rs#; gnomAD: absent	-	-	-	-	-	-100.00%	0.00%	-100.00%
57949199	23	c.2258T>A	p.(Leu753 *)	Premature stop codon leading to a shorter protein product with only the N-terminus fragment or NMD	no rs#; gnomAD: absent	-	-	-	Disease Causing (1)	-	-	-	-
57949173	23	c.2284C>T	p.(Arg762 Cys)	Linker TD3-TD4	rs1028371920; gnomAD: 0.0007% (2/280610/0)	1,58	180	Deleterious (0)	Disease Causing (1)	Probably Damaging (1)	-	-	-
57949172	23	c.2285G>A	p.(Arg762 His)	Linker TD3-TD4	rs760373259; gnomAD: 0.0016% (4/249018/0)	5,29	29	Deleterious (0)	Disease Causing (1)	Probably Damaging (1)	-	-	-
57949164	23	c.2293C>T	p.(Arg765 Cys)	Linker TD3-TD4	rs771833874; gnomAD: 0.002% (5/249044/0)	5,29	180	Deleterious (0)	Disease Causing (1)	Probably Damaging (1)	-	-	-
57949163	23	c.2294G>T	p.(Arg765 Leu)	Linker TD3-TD4	no rs#; gnomAD: absent	5,29	102	Deleterious (0)	Disease Causing (1)	Probably Damaging (1)	-	-	-
57946900	IVS23	c.2305-2A>G	p.?	Possible effect on splicing leading to a shorter/longer protein product or NMD	no rs#; gnomAD: 0.0004% (1/249138/0)	-	-	-	-	-	-100.00%	-100.00%	-100.00%
57912979	24	c.2320G>A	p.(Glu774 Lys)	Linker TD3-TD4	rs1286857064; gnomAD: 0.0004% (1/249434/0)	7,64	56	Tolerated (0.09)	Disease Causing (1)	Possibly Damaging (0.810)	-	-	-
57946850	24	c.2353A>T	p.(Lys785 *)	Premature stop codon leading to a shorter protein product with only the N-terminus fragment or NMD	no rs#; gnomAD: absent	-	-	-	Disease Causing (1)	-	-	-	-

57946842	24	c.2361C>A	p.(Tyr787*)	Premature stop codon leading to a shorter protein product with only the N-terminus fragment or NMD	rs367678786; gnomAD: 0.0012% (3/249544/0)	-	-	-	Disease Causing (1)	-	-	-	-
57945656	IVS25	c.2492+1G>A	p.?	Possible effect on splicing leading to a shorter/longer protein product or NMD	rs530551814; gnomAD: absent	-	-	-	-	-	-100.00%	-100.00%	-100.00%
57911751	IVS25	c.2492+2T>G	p.?	Possible effect on splicing leading to a shorter/longer protein product or NMD	no rs#; gnomAD: absent	-	-	-	-	-	-100.00%	-100.00%	-100.00%
57938777	IVS25	c.2493-2_2495delinsG GC	p.?	Possible effect on splicing leading to a shorter/longer protein product or NMD	no rs#; gnomAD: absent	-	-	-	Disease Causing (1)	-	-100.00%	-100.00%	-100.00%
57938781	IVS25	c.2493-2A>G	p.?	Possible effect on splicing leading to a shorter/longer protein product or NMD	rs745319716; gnomAD: 0.002% (5/249394/0)	-	-	-	-	-	-100.00%	-100.00%	-100.00%
57938771	26	c.2501G>T	p.(Arg834 Leu)	Linker TD4-TD5	rs761295014; gnomAD: 0,0014% (4/280872/0)	5,69	102	Deleterious (0)	Disease Causing (1)	Possibly Damaging (0.801)	-	-	-
57938764	26	c.2508C>A	p.(Tyr836*)	Premature stop codon leading to a shorter protein product with only the N-terminus fragment or NMD	no rs#; gnomAD: 0.0011% (3/280910/0)	-	-	-	Disease Causing (1)	-	-	-	-
57938748	26	c.2524dup	p.(Thr842 Asnfs*10)	Premature stop codon leading to a shorter protein product with only the N-terminus fragment or NMD	rs527236061; gnomAD: absent	-	-	-	-	-	-	-	-



57938732	26	c.2540G>A	p.(Gly847 Glu)	Linker Pore-TD6	no rs#; gnomAD: 0.0008% (2/249580/0)	5,69	98	Deleterious (0)	Disease Causing (1)	Probably Damaging (1)	-	-	-
57938730	26	c.2542_2543ins A	p.(Gly848 Glufs*4)	Linker Pore-TD6	no rs#; gnomAD: absent	-	-	-	Disease Causing (1)	-	-	-	-
57938728	26	c.2544dup	p.(Leu849 Alafs*3)	Premature stop codon leading to a shorter protein product with only the N-terminus fragment or NMD	rs760430056; gnomAD: (0.0036% 10/280958/0)	-	-	-	Disease Causing (1)	-	-	-	-
57938727	26	c.2545dup	p.(Leu849 Profs*3)	Premature stop codon leading to a shorter protein product with only the N-terminus fragment or NMD	no rs#; gnomAD: absent	-	-	-	Disease Causing (1)	-	-	-	-
57938717	26	c.2555C>T	p.(Pro852 Leu)	TD6	rs768202610; gnomAD: 0,0014% (4/280960/0)	5,69	98	Deleterious (0)	Disease Causing (1)	Probably Damaging (1)	-	-	-
57938697	26	c.2575G>A	p.(Val859Ile)	TD6	rs1308416277; gnomAD 0,0007% (2/280982/0)	0,85	29	Tolerated (0.33)	Disease Causing (0.989)	Benign (0.057)	-	-	-
57938669	26	c.2603G>A	p.(Gly868 Asp)	TD6	rs770961534; gnomAD: 0,0008% (2/249582/0)	4,16	94	Deleterious (0)	Disease Causing (1)	Probably Damaging (1)	-	-	-
57937858	26	c.2662G>A	p.(Ala888 Thr)	TD6	rs368328328; gnomAD: 0,022% (63/280510/0)	2,87	58	Tolerated (0.17)	Disease Causing (1)	Possibly Damaging (0.722)	-	-	-
57937844	27	c.2676C>A	p.(Tyr892*)	Premature stop codon leading to a shorter protein product with only the N-terminus fragment or NMD	no rs#; gnomAD: absent	-	-	-	Disease Causing (1)	-	-	-	-
57937839	27	c.2681G>A	p.(Arg894 His)	C-linker	rs146762538; gnomAD: 0.0442% (124/280786/0)	5,53	29	Deleterious (0.01)	Disease Causing (1)	Possibly Damaging (0.953)	-	-	-
57937760	27	c.2760G>A	p.(Trp920*)	Premature stop codon leading to a shorter protein	rs776312649; gnomAD: 0.0008% (2/249494/0)	-	-	-	Disease Causing (1)	-	-	-	-

				product with only the N-terminus fragment or NMD										
57937755	27	c.2762_2765del	p.(Tyr921 Cysfs*15)	Premature stop codon leading to a shorter protein product with only the N-terminus fragment or NMD	no rs#; gnomAD: absent	-	-	-	Disease Causing (1)	-	-	-	-	-
57937757	27	c.2763C>G	p.(Tyr921 *)	Premature stop codon leading to a shorter protein product with only the N-terminus fragment or NMD	no rs#; gnomAD: absent	-	-	-	Disease Causing (1)	-	-	-	-	-
57935256	28-29	c.2777-?_2958+?del	p.?	Premature stop codon leading to a shorter protein product with only the N-terminus fragment or NMD	no rs#; gnomAD: absent	-	-	-	Disease Causing (1)		0.00%	0.00%	0.00%	
57937725	IVS27	c.2794+1G>A	p.?	Possible effect on splicing leading to a shorter/longer protein product or NMD	rs770011113; gnomAD: 0.0092% (23/249286/0)	-	-	-	-	-	-100.00%	-100.00%	-100.00%	
57935519	28	c.2805del	p.(Glu935 Aspfs*2)	Premature stop codon leading to a shorter protein product with only the N-terminus fragment or NMD	no rs#; gnomAD: 0.0008% (2/249354/0)	-	-	-	Disease Causing (1)	-	-	-	-	-
57935457	28	c.2867del	p.(Ile956T hrfs*15)	Premature stop codon leading to a shorter protein product with only the N-terminus fragment or NMD	rs1231250334; gnomAD: 0.0008% (2/249570/0)	-	-	-	Disease Causing (1)	-	-	-	-	-
57935435	28	c.2888_2889del	p.(Phe963 Serfs*4)	Premature stop codon leading to a shorter protein product with only	no rs#; gnomAD: absent	-	-	-	Disease Causing (1)	-	-	-	-	-

57935346	IVS28	c.2893-7G>A	p.?	the N-terminus fragment or NMD Possible effect on splicing leading to a shorter/longer protein product or NMD	rs749199721; gnomAD: 0.005% (14/280976/0)	-	-	-	-	-	-54.70%	0.50%	-100%
57935339	29	c.2893G>A	p.(Gly965 Ser)	C-linker; Possible effect on splicing leading to a shorter/longer protein product or NMD	rs559591083; gnomAD: absent	4,08	56	Tolerated (0.08)	Disease Causing (1)	Possibly Damaging (0.866)	-15.70%	-77.50%	-5.40%
57935311	29	c.2921T>G	p.(Met974 Arg)	CNBD	Rs752967885; gnomAD: 0.0035% (10/280974/0)	3,19	91	Deleterious (0)	Disease Causing (1)	Probably Damaging (0.988)	-	-	-
57935275	29	c.2957A>T	p.(Asn986 Ile)	CNBD	rs201162411; gnomAD: 0.1182% (332/280924/0)	3,27	149	Deleterious (0.01)	Disease Causing (1)	Probably Damaging (0.983)	-	-	-
57935266	29	c.2966T>A	p.(Val989 Glu)	CNBD	rs201162411; gnomAD: 0.0014% (4/280866/0)	4,73	121	Deleterious (0)	Disease Causing (1)	Possibly Damaging (0.998)	-	-	-
57931817	30	c.2978G>T	p.(Gly993 Val)	CNBD	rs121918532; gnomAD: absent	5,94	109	Deleterious (0.01)	Disease Causing (1)	Probably Damaging (1)	13.10%	0.30%	0.00%
57931815	30	c.2980G>T	p.(Glu994 *)	Premature stop codon leading to a shorter protein product with only the N-terminus fragment or NMD	no rs#; gnomAD: absent	-	-	-	Disease Causing (1)	-	0.00%	-0.20%	0.00%
57931745	30	c.3044_3050del	p.(Gly1015Valfs*4)	Premature stop codon leading to a shorter protein product with only the N-terminus fragment or NMD	no rs#; gnomAD: absent	-	-	-	Disease Causing (1)	-	-	-	-
57931394	30	c.3131_3149del	p.(Ala1044Glyfs*13)	Premature stop codon leading to a shorter protein product with only	rs1365926616; gnomAD: 0.0014% (4/280916/0)	-	-	-	Disease Causing (1)	-	-	-	-

				the N-terminus fragment or NMD										
57931401	31	c.3139_3142dup	p.(Ala1048Glyfs*13)	Premature stop codon leading to a shorter protein product with only the N-terminus fragment or NMD	rs756806434; gnomAD: 0.0036% (10/280876/0)	-	-	-	Disease Causing (1)	-	-	-	-	-
57931393	31	c.3150del	p.(Phe1051Leufs*12)	Premature stop codon leading to a shorter protein product with only the N-terminus fragment or NMD	rs753353134; gnomAD: 0.0014% (4/280902/0)	-	-	-	Disease Causing (1)	-	-	-	-	-
57921758	IVS32	c.3462+1G>A	p.[=;Arg1081Argfs*68]†	Possible effect on splicing leading to a shorter/longer protein product or NMD	no rs#; gnomAD: absent	-	-	-	-	-	-100.00%	-100.00%	-100.00%	-100.00%

#: Effect validated by means of minigene assay in (Saqib et al., 2015). †: Effect validated by means of minigene assay by (Becirovic et al., 2010). ‡: Effect validated by means of *in vitro* assay by (Petersen-Jones et al., 2018)

**Table S2.** *CNGB1* conservation analysis (without GARP domain) on homologous genes performed using the Alignment tool on UniProt (available at: <https://www.uniprot.org/align/>). The novel missense variants found in the study are highlighted in red.

Q14028   CNGB1_H.SAPIENS	EEEEEEEEEEVTEVLLDSCVVSQVGVGQSEEDGTRPQSTSDQKLWEEVGEAAKKEAEEK	60
Q9NQW8   CNGB3_H.SAPIENS	-----MFKSLT-KVNKVKPIGENNENEQSSR-----	25
Q9JJZ9   CNGB3_M.MUSCULUS	-----MLKSLTVKFNKVNPMEGRMEKK-----	22
Q8MJD7   CNGB3_C.LUPUS	-----MFKSLTIKSNKVKPREENDEN-----	21
W5PPU7   CNGB3_O.ARIES	-----	
A0A1D5PGA2   CNGB3_G.GALLUS	-----	
A0A2R8RTW7   cngb3.2_D.RERIO	-----	
A0A0R4IL01   cngb3.1_D.RERIO	-----	
G5EEE2   tax-2_C.ELEGANS	-----MYQ-VPKRAK-----	9
Q14028   CNGB1_H.SAPIENS	AKEEAEEVAEEEEAEKEPQDWAETKE--EPEAEAEAASSGVDPATKQHP-EVQVEDTDADSC	117
Q9NQW8   CNGB3_H.SAPIENS	-----RNEE--GSHPS----NQSQQTTAQEENKGEKSLKTKST	58
Q9JJZ9   CNGB3_M.MUSCULUS	-----L--CPNLS----SLSQPTIAQGDNQSEKEPLR-SRT	51
Q8MJD7   CNGB3_C.LUPUS	-----KQ--DPDPS----NQPQQSTRQGENKSENKSLQTKMT	52
W5PPU7   CNGB3_O.ARIES	-----	
A0A1D5PGA2   CNGB3_G.GALLUS	-----AHC	3
A0A2R8RTW7   cngb3.2_D.RERIO	-----VSSFIRKILAAAPEPAAP-AKEPEPAAAKEPEQA-----A	34
A0A0R4IL01   cngb3.1_D.RERIO	-----P-----A	2
G5EEE2   tax-2_C.ELEGANS	-----TNLARE-IRKREFSYVDRQKA-----SKPTQLSEKEWKSP-----	43
Q14028   CNGB1_H.SAPIENS	PLMAEENPPSTVLPSPAKSDTLIVPSSASGTHRKK--LPSEDD-EAEELKALSPAESP	174
Q9NQW8   CNGB3_H.SAPIENS	PVTSEEPHTN-----IQDKLSKK--NS--SGDLTTNPDQON-AAEPTGTVPQEKEM	104
Q9JJZ9   CNGB3_M.MUSCULUS	PITFEKSHSK-----E-DNSTGE--NS--LRDFTPNPDPEC-RAELTRTMAEMEKT	96
Q8MJD7   CNGB3_C.LUPUS	PVTFEESHAK-----MQDKISEK--NS--LRDLTTNPNHQH-PTESKGAMSEQEM	98
W5PPU7   CNGB3_O.ARIES	-----	
A0A1D5PGA2   CNGB3_G.GALLUS	WLTFSCSTN-----TSRSISSA--QSSSHSSLQRSPNAWQ-----SWLA----L	42
A0A2R8RTW7   cngb3.2_D.RERIO	P--AKEPE-----PAAPAKEPEPA-----APAPAK-EPEP-AAPAPAKEP	70
A0A0R4IL01   cngb3.1_D.RERIO	P--GSAPA-----PA-----P-----APAPGS-APAP----APASAP	27
G5EEE2   tax-2_C.ELEGANS	----RSEDSFDLLDPANASKEPSAS-----TR---PLPYPTRPPEVVIQIDEVESP	88

Q14028 CNGB1_H.SAPIENS	V-VAW-----SDPTTPKDTDGQDR-----AASTASTNSAIINDRLQELVKLF	216
Q9NQW8 CNGB3_H.SAPIENS	DPGK-----EGPNSP-----QN-----KPPAAPVINEYADAQLHNLVKRM	139
Q9JJZ9 CNGB3_M.MUSCULUS	RTGK-----ERPVSF-----KT-----KVLETSIINEYTD AHLHNLVERM	131
Q8MJD7 CNGB3_C.LUPUS	ETGK-----EGLVSP-----KS-----KPLGVPVINEYADAQLHNLVRRM	133
W5PPU7 CNGB3_O.ARIES	-----H-----PKSKSPVINEYADAQLHSLVRRL	24
A0A1D5PGA2 CNGB3_G.GALLUS	QNGLC-----LHSNNT-----QN-----ATSQGFQTNEYADAQLQEIVRKM	78
A0A2R8RTW7 cngb3.2_D.RERIO	---EP-----AAPAPAAKPEGTPA-----DPPRPILISEEIDTHLIEMIQKL	109
A0A0R4IL01 cngb3.2_D.RERIO	APAPA-----SAPAPAPAEDGPPS-----PPTPPVYYRYTDDQLRDIVKKM	69
G5EEE2 tax-2_C.ELEGANS	ILGLIDETDDHELDGRLLDPASSFDANSLSATRASSIIEDDVRSQISFIMRERLHSIAKEV	148

Q14028 CNGB1_H.SAPIENS	KERTEKVKEKLIDPDV-TSDEESPKPSPAKKAPEP-----A---	250
Q9NQW8 CNGB3_H.SAPIENS	RQRTALYKKKLVEGD-LSSPEASPQTAKPTAV-----	170
Q9JJZ9 CNGB3_M.MUSCULUS	RERTALYKKTLEENFPEVEASSQTAMSTNI-----	163
Q8MJD7 CNGB3_C.LUPUS	RQRTMLYKKKLAEGD-ISSPEASPQTAKPTAV-----	164
W5PPU7 CNGB3_O.ARIES	RQRTDFYKRKLVEAD-MSSPESSPQTAKPTAV-----	55
A0A1D5PGA2 CNGB3_G.GALLUS	RERATAYKEKLDKDPV-LSSPEGSPTPPPPPKKEKK-----E---	113
A0A2R8RTW7 cngb3.2_D.RERIO	RQRTEQFKEKVIDPY-ASSPERSPPVTPVLRKDDYYKKRQEEEEERIRKEEE-KKRKEEEA	167
A0A0R4IL01 cngb3.2_D.RERIO	RRETELYKDKIVDPY-ASSPERTPPVTPVYRKEDWIRKQEEE--RIKREEAEQKKKEDDA	126
G5EEE2 tax-2_C.ELEGANS	HRRTSAVREDLIRET----PEDTVSM--ASNV-----	174

Q14028 CNGB1_H.SAPIENS	-----PDTKPAAEAPVE-----EEHY--CDMLCCKFKHRPWKKY	282
Q9NQW8 CNGB3_H.SAPIENS	-----P-PVKESDDK-P-----TEHY--YRLLWFKVKKMPLTEY	200
Q9JJZ9 CNGB3_M.MUSCULUS	-----S-PKQENNSKLLK-----EHQ---DTFSFKPQRPVKEH	192
Q8MJD7 CNGB3_C.LUPUS	-----P-STQESSAKLLK-----EEHY--YHILCFKFQKMPLETEY	195
W5PPU7 CNGB3_O.ARIES	-----S-STQESSAKLLK-----EEHS-----QKAPLIEY	78
A0A1D5PGA2 CNGB3_G.GALLUS	-----E-KKEEAEAKPE-----EDHY--CDMLCCKFKKPLPKKY	144
A0A2R8RTW7 cngb3.2_D.RERIO	KKKKEEAEKKKKEEKKKKEEKKKKEEKKK--KKEQAGKPK--KSIFSKVNFTCVDFVLKPFEMR	223
A0A0R4IL01 cngb3.2_D.RERIO	KRAAA--KKEKEEKEKKEEKKLKAKEEAADKEAA--EAMFPKIKCTCIDTLLKPFEDK	181
G5EEE2 tax-2_C.ELEGANS	-----PKQNEHRP-S-----LMSLIGLQNRSESPVDTVKNCFGF-----	208

p. (S647R)

Q14028 CNGB1_H.SAPIENS	----QFPQSIDPLTNLMYVLWLVFFVVMAWNWCWLI PVRWAFPYQTPDNIHHWLLMDYLC	338
Q9NQW8 CNGB3_H.SAPIENS	LKRIKLPNSIDSYTDRLYLLWLLLVTLAYNWNCCFIPLRLVFPYQTADNIHYWLIADIIC	260
Q9JJZ9 CNGB3_M.MUSCULUS	LRRMILPRSIDSYTDRLYLLWLLLVTIAYNWNWCWLLPVRLVFPYQTPDNKNYWIITDIVC	252
Q8MJD7 CNGB3_C.LUPUS	LKRFRLPGSIDSYTDRLYLLWLLLVTIAYNWNWCWLIPLRLVFPYQTPDNTHYWFITDITC	255
W5PPU7 CNGB3_O.ARIES	LKRLRLPKSIDSYTDRLYLLWLLLVTIAFNWNCWFIPLRMVFPYQTPHNTHYWLITDLVC	138
A0A1D5PGA2 CNGB3_G.GALLUS	MTYLKLPDSIDSYTDRLYVAVLMLVTVAYNWNWCWFIPLRFVFPYQTPSNTIYWFAIDIIC	204
A0A2R8RTW7 cngb3.2_D.RERIO	M-DNRIGKSIDPFTDRRYITWLSMVTIAFNYNLWFVPVRMAFPYHSPEVVPLWFTLDIIA	282
A0A0R4IL01 cngb3.2_D.RERIO	M-DSYLGATIDPFTDRRYIKWLSVVTVAFNYNVWLATARLCFPYHTPATIPFWILFDFLA	240
G5EEE2 tax-2_C.ELEGANS	----SLKGTTFHPY-GRFYMTWLSLVTLCFLFNAFCIPLRSSYPYQTPADNWMYWFIVDYSC	263

Q14028 CNGB1_H.SAPIENS	DLIYFLDITVVFQTRLQFVRGGDIITDKKDMRNNYLKSRRFKMDLLSLLPLDFLYLKVGVN	398
Q9NQW8 CNGB3_H.SAPIENS	DIIYLYDMLFIQPRQLQFVRGGDIIVDSNELRKHYRTSTKFQLDVASIIPFDICYLFFGFN	320
Q9JJZ9 CNGB3_M.MUSCULUS	DIIYLCDILLIQPRQLQFVRGGEIIVDSNELKRNYRSSTKFRMDVASLLPFEVLYIFFGVN	312
Q8MJD7 CNGB3_C.LUPUS	DIIYLCDMLLIQPRQLQFIKGGDIMVDSNELKRHYRSSTKFQLDVASVMPFDVLYLFFGFN	315
W5PPU7 CNGB3_O.ARIES	DTIYLFDLLLIQPRQLQFMRGGDIIVDSNELKRHYRNSTKFQLDMASIMPFDVLYLFFGFN	198
A0A1D5PGA2 CNGB3_G.GALLUS	DICYLCDLLVQPRVQFLRGGDIISDKVEMKKFYHSTIKFRLDLISVLPFDVLYFFFGFN	264
A0A2R8RTW7 cngb3.2_D.RERIO	DFIYIFDMIFFQPRQLQFSKGGDIIDREVIVKIKKYRESGRFQNDVIAVLPIDLLYIPFGFN	342
A0A0R4IL01 cngb3.2_D.RERIO	DLVNVIDITMFQPRQLQFVKAGDIKDRVQTKQNYRESARFQTDLISIIIPFDLLCFQFGFT	300
G5EEE2 tax-2_C.ELEGANS	DLVYVIDMLLIKPRLRFTRGGIQVKIYKDTQRHYLMTRTFKLDILSILPTDLMYFFFGKM	323

p. (E774K)

Q14028 CNGB1_H.SAPIENS	PLLRPRCLKYMAFFEFNSRLESILSKAYVYRVIRTTAYLLYSLHLNSCLYYWASAYQGL	458
Q9NQW8 CNGB3_H.SAPIENS	PMFRANRMLKYTSFFEFNHHLESIMDKAYIYRVIRTTGYLLFILHINACVYYWASNYEGI	380
Q9JJZ9 CNGB3_M.MUSCULUS	PIFRANRILKYTSFFEFNHHLESIMDKAYVYRVIRTTGYLLFLLHINACVYYWASDYEGI	372
Q8MJD7 CNGB3_C.LUPUS	PVFRMNRILKYTSFFEFNHHLESIMDKAYIYRVIRTTGYLLYTLHINACIYYWASDYEGI	375
W5PPU7 CNGB3_O.ARIES	PIFRNRMLKYTSFFEFNHHLESIMNKAYIYRVIRTTGYLLFTLHINACMYWASSYEGI	258
A0A1D5PGA2 CNGB3_G.GALLUS	PAFRVNRMLKHNTFFEFNDRLEAILDKAYIYRVIRTTGYLLFILHINACLYWASDYEGL	324
A0A2R8RTW7 cngb3.2_D.RERIO	SVFRLNRLMKVESFFEFSDRLEGLLTRAYIWRVIRTTGYLLFILHLNACLYWASVSQGI	402
A0A0R4IL01 cngb3.2_D.RERIO	SFFRLNRFMRYSFFEFSDRLESIMAKAYIWRVGRRTGYLLYCLHINSCLYYVASEYEGE	360
G5EEE2 tax-2_C.ELEGANS	PIWRINRVLKINSFWLLFDMLDNSFANPYAIRIARTLSYMIYIIHCNSCVYYKLSALQAF	383

	p. (R834L)	p. (P852L)	p. (V859I)	
Q14028 CNGB1_H.SAPIENS	GS-----THWVYDGVGNS-YI	RCYYFAVKTLITIGGLPDE	PKTLFEIVFQLLNYF	506
Q9NQW8 CNGB3_H.SAPIENS	GT-----TRWVYDGEENE-YL	RCYYWAVRTLITIGGLPEP	QTLFEIVFQLLNFF	428
Q9JJZ9 CNGB3_M.MUSCULUS	GS-----TKWVYNGEGNK-YL	RCFYWAVRTLITIGGLPEP	QTSFEIVFQFLNFF	420
Q8MJD7 CNGB3_C.LUPUS	GS-----TKWVYNGEGNK-YL	RCYYWAVRTLITIGGLPEP	QTSFEIVFQLLNFF	423
W5PPU7 CNGB3_O.ARIES	GS-----TRWVYDGEENKWL	RCYYWAVRTLITIGGLPEP	QTLFEIVFQLLNFF	307
A0A1D5PGA2 CNGB3_G.GALLUS	GS-----TRWVYDGQGNM-YL	RCYYWAVRTLITIGGLPEP	QTLFEIVFQLLNFF	372
A0A2R8RTW7 cngb3.2_D.RERIO	GS-----TKWVYSGKGS-A-YL	HSYYFAVRTLINIGGLPEP	HTIFEISFQLTNFF	450
A0A0R4IL01 cngb3.2_D.RERIO	GS-----SRWTYDGLGNA-YL	RCYYFATRTLITIGGLPEP	HTLFEIVFQLVNFF	408
G5EEE2 tax-2_C.ELEGANS	GQIAYLENGKWYLNKWVYNNQ	GNA-YI	RCFYFTAAVATSTGNNPA	PTNVIEYTYMTCSWM 442

	p. (G868D)	p. (A888T)	
Q14028 CNGB1_H.SAPIENS	TGVFAFSVMIGQMRDVGAATA	AGQTYRSCMDSTVKYMN	FYKIPKSVQNRVKTWYEYTW 602
Q9NQW8 CNGB3_H.SAPIENS	SGVVFVSSLIGQMRDVIGAATA	NQNYFRACMDDTIAYMNN	YSIPKLVQKRVRTWYEYTD 488
Q9JJZ9 CNGB3_M.MUSCULUS	SGVVFVSSLIGQMRDVIGAATA	NQNYFQACMDHIIAYMN	KYSIPQSVQYRVRTWLEYTN 480
Q8MJD7 CNGB3_C.LUPUS	SGVVFVSSLIGQMDDVIGAATA	NQNNFRISMDHTISYMNT	YSIPKQVQNRVRTWYEYTD 483
W5PPU7 CNGB3_O.ARIES	SGVVFVSSLIGQMDDVIGAATA	NQNNFRICMDHTIAYMNT	YSIPKIVQNRVRTWYEYTW 367
A0A1D5PGA2 CNGB3_G.GALLUS	LCVVFVSSLIGQMRDVIGAATA	AGQNYRSCMDNTVSYMNT	YSIPKLVQNRVRTWYEYTD 432
A0A2R8RTW7 cngb3.2_D.RERIO	VGVVFVSSLIGQMRDVIGAATA	AGQTYFRASMDACVAYM	VTNHIIPKMVQSRVRTWYNYTD 510
A0A0R4IL01 cngb3.2_D.RERIO	TGVVFVSSLIGQMRDVIGAATA	AGQTYFRASMDSCVAYM	NTYTIIPKLVQSRVRTWYNYTD 468
G5EEE2 tax-2_C.ELEGANS	MGVVFVALLLQIRDIVSNAN	RNREEFQRKMDLALGECK	KLGLKMETTNRVRDWFYITWQ 502

Q14028 CNGB1_H.SAPIENS	SQGMLDESELMVQLPDKMRLDLA	IDVNINIVSKVALFQGC	DRQMI FDKMLKRLRSVYLPN 626
Q9NQW8 CNGB3_H.SAPIENS	SQRMLDESDLLKTLPTTVQLALA	IDVNFSIIISKVDLFGC	DTQMIYDMLLRKLSVLYLPG 548
Q9JJZ9 CNGB3_M.MUSCULUS	SQRILDESNLLENLPTAMQLS	IALDINFSSIIDKVELFKG	CDTQMIYDLLLLRLKSTIYLPG 540
Q8MJD7 CNGB3_C.LUPUS	SQRMLDESDLLCTLPTTMQLALT	VDVNLSIIISKVELFKG	CDTQMIYDMLLRKSTVYLPG 543
W5PPU7 CNGB3_O.ARIES	SQRMLDESDLLETLPPTMQLALT	VDNFGVVISKVDLFGC	DTQMIYDMLLRKLSIVYLPG 427
A0A1D5PGA2 CNGB3_G.GALLUS	SQGMLDESELLEQMPTKMLAIA	IDVNFAIVNKVDLFGC	DTQMIYDMLLRKLSIVYLPG 492
A0A2R8RTW7 cngb3.2_D.RERIO	SQGMLDESELLGQMPLVMRTA	IAVDINLATFQKIELFKG	CDNQMMLVDMLLRKLSIVYLPG 570
A0A0R4IL01 cngb3.2_D.RERIO	SQGMLDESELLDKMPLVMRTA	IAVDINLATFQKIDL	FKGCDNQMMLVDMLLRKLSIVYLPG 528
G5EEE2 tax-2_C.ELEGANS	QQKTLDEKKLIEKLPKLQTD	LALSVHYTTLSKVQLFQ	DCDRALLRDLVLRPVIIFLPG 562



p. (V989E)

Q14028 CNGB1_H.SAPIENS	DYVCKKGEIGREMYIIQAGQVQVLGGPDGKSVLVTLKAGSVFGEISLLA--VGGGNRRTA	684
Q9NQW8 CNGB3_H.SAPIENS	DFVCKKGEIGKEMYIIKHGEVQVLGGPDGKTVLVTLKAGSVFGEISLLA--AGGGNRRTA	606
Q9JJZ9 CNGB3_M.MUSCULUS	DFVCKKGEIGKEMYIIKHGEVQVLGGPDGAQVLVTLKAGSVFGEISLLA--KGGGNRRTA	598
Q8MJD7 CNGB3_C.LUPUS	DFVCKKGEIGKEMYIIKQGEVQVLGGSDGAQVLVTLKAGAVFGEISLLA--GRGGNRRTA	601
W5PPU7 CNGB3_O.ARIES	DFVCKKGEIGKEMYIIKQGEVQVLGGADGTQVLVTLKAGAVFGEISLLA--ARGGNRRTA	485
A0A1D5PGA2 CNGB3_G.GALLUS	DFVCKKGEIGREMYIIKQGEVQVLGGPDGKTVLVTLRAGAVFGEISLLA--AGGGNRRTA	550
A0A2R8RTW7 cngb3.2_D.RERIO	DFVVKKGDIGKEMYIIKAGEVQVIGGPDNKIVFVTLKAGCVFGEISLLQSSANGGNRRTA	630
A0A0R4IL01 cngb3.2_D.RERIO	DFVCKKGDIGREMYIIKAGEVQVIGGPDNKIVFVTLKAGCVFGEISLLQSAKDGGNRRTA	588
G5EEE2 tax-2_C.ELEGANS	DMICLKGDVKGEMYIINQGILQVVGGDHNEKIFAELAQQGAVFGEISLLA--IGGNRRTA	620

Q14028 CNGB1_H.SAPIENS	NVVAHGFTNLFILDKKDLNEILVHYPESQKLLRKKARRMLRSNNK-----PKEEK	734
Q9NQW8 CNGB3_H.SAPIENS	NVVAHGAFANLLTLDKKTQLEIILVHYPDSERILMKKARVLLKQKAKT-----AEATPPRKD	661
Q9JJZ9 CNGB3_M.MUSCULUS	DVVAHGAFANLLTLDKKTQLEIILLHYPTSKLLMKKAKILLSQKGT-----TQAI PARPG	653
Q8MJD7 CNGB3_C.LUPUS	NVIAHGAFANLLTLDKKTQLEIILVHYPDSEKLLMKKASVLLKKA-----TETTPPRKG	656
W5PPU7 CNGB3_O.ARIES	NVVAHGAFANLLTLDKKTQLEIILVHYPDSEKLLMKKARVLLKNKAPG-----TGATPPNKG	540
A0A1D5PGA2 CNGB3_G.GALLUS	NVVAHGAFANLFI LDKKTLNEILVHYPDSEKLLMKKAKYVLRITIFKSLCLDCKWTVVQPRG	610
A0A2R8RTW7 cngb3.2_D.RERIO	NVAAHGAFANL FVLDKKDLNDILIHYPESQKVLARKGRKLLKAKGPPPAKA---DEEKKK	687
A0A0R4IL01 cngb3.2_D.RERIO	NVAAHGAFANL FVLDKKDLNDILIHYPESQKVLAKKGRKLMKAKGKAAPT KD---EGEKKK	645
G5EEE2 tax-2_C.ELEGANS	SIRAKGYCTLFVLAKEDLNDVIRYYPQAQTILRRKAAAMLKNDKKSDEKTEKIKAQAELE	680

Q14028 CNGB1_H.SAPIENS	SVLILPPRAGTPKLFNAALAMTGKMGKG-----AKGGKLAHLRRLKELAALEAAA	786
Q9NQW8 CNGB3_H.SAPIENS	LALLFPPKEETPKLFKTLLGGTGKASLAR-----LLKLRQAAQKKENSEGEGEEG	713
Q9JJZ9 CNGB3_M.MUSCULUS	PAFLFPPKEETPRMLKVLLGNTGKVDLGR-----LLKGRKTTTQK-----	694
Q8MJD7 CNGB3_C.LUPUS	LAFLFPPKQETPKIFKALLGGTGKAGLTR-----LLKLRQETIQKTSSENS-----	702
W5PPU7 CNGB3_O.ARIES	LAFLFPPKQETPKMFKALLGSSGKAGLAR-----LLTLKREQTGQRKDENQ-----	586
A0A1D5PGA2 CNGB3_G.GALLUS	LASLFGQKQETPKLKFAMFGAKGKGLAK-----LLQLKREQDIQVMSQIIIEQILSR	662
A0A2R8RTW7 cngb3.2_D.RERIO	GLALFGQKPPTPKMLRAFNVVHNI STSH-----	715
A0A0R4IL01 cngb3.2_D.RERIO	GLALFGPKPPTPKMLQCYVYTHIRKLHVNASAFASYSLLLSTFERSRVRVRFVTHTLNSN	705
G5EEE2 tax-2_C.ELEGANS	DRCKINPR-QVPKLITLIANMTEMNENKGVQE-----LKKVIE-----EETEKSR	724

Q14028 CNGB1_H.SAPIENS	KQQELVEQAKSSQD-----VKGEEGSAAPDQHTHPKEAATDPPAPRTPPEPPGSPSSPP	841
Q9NQW8 CNGB3_H.SAPIENS	KEN--EDKQKENEDKQKENEDKDKGREPEEKPLDRPECTASPIAVEEEP-----	767
Q9JJZ9 CNGB3_M.MUSCULUS	-----	
Q8MJD7 CNGB3_C.LUPUS	-----EEGGGKRREYEDKEREPESEKILDSSECRANCIIAEEMP-----	740
W5PPU7 CNGB3_O.ARIES	-----EEE-DKGKESDKGRATAEKPLEASKCQTSPITAEAP-----	623
A0A1D5PGA2 CNGB3_G.GALLUS	-----	
A0A2R8RTW7 cngb3.2_D.RERIO	-----	
A0A0R4IL01 cngb3.2_D.RERIO	IYNYRF----YSTALH---F-----	718
G5EEE2 tax-2_C.ELEGANS	RQSIYYPWSTLQRD----DDDEEWNDEEDLSDVGEDFDLDPTNHSDDDEDPMEDVDLAPE	780

Q14028 CNGB1_H.SAPIENS	PASLGRPEGEEEGPAEPEEHSVRCMSPGPEPGEQILSVKMPEEREKAE	891
Q9NQW8 CNGB3_H.SAPIENS	-HSV----RRTVLPRGTSRQSLIISMPSAEGGEEVLTIEVKEKAKQ---	809
Q9JJZ9 CNGB3_M.MUSCULUS	-----	
Q8MJD7 CNGB3_C.LUPUS	-QSI----RRAALPRGTTRQSLIISMPSAEGGEEVLTIEVKEKAKQ---	782
W5PPU7 CNGB3_O.ARIES	-QAI----RKAVLPRGTTRQSLIISMPSAEGGEEVLTIEVKEKAKQ---	665
A0A1D5PGA2 CNGB3_G.GALLUS	-----	
A0A2R8RTW7 cngb3.2_D.RERIO	-----	
A0A0R4IL01 cngb3.2_D.RERIO	-----	
G5EEE2 tax-2_C.ELEGANS	VHDD---DWDQPGTSGT--QKLHAD-----	800

**Table S3.** Conservation analysis of the novel missense variants on *CNGB1*, described in the study. This analysis was performed using the University of California Santa Cruz (UCSC) Genome Browser, available at <https://genome.ucsc.edu/index.html>. The interested residue is highlighted in red

Nucleotide Genomic position (hg19)	57953019	57912979	57938771	57938717	57938697	57938669	57937858	57935266
AA position	647	774	834	852	859	868	888	989
Altered residue	R	K	L	L	I	D	T	E
<i>H.sapiens</i>	YQFPQSIDPLT	YMAFFEFNSRL	NGSYIRCYIFA	GGLPDEKTLFE	TLFEIVFQLLN	LNYFTGVFAFS	VGAATAGQTY	LPNDYVCKKGE
<i>P.troglodytes</i>	YQFPQSIDPLT	---	NGSYIRCYIFA	GGLPDEKTLFE	TLFEIVFQLLN	LNYFTGVFAFS	VGAATAGQTY	LPNDYVCKKGE
<i>M.mulatta</i>	YQFPQSIDPLT	YMAFFEFNNRL	NGSYIRCYIFA	GGLPDEKTLFE	TLFEIVFQLLN	LNYFTGVFAFS	VGAATAGQTY	LPNDYVCKKGE
<i>R.norvegicus</i>	YQFPQSIDPLT	YMAFFEFNNRL	NGSYIRCYIWA	GGLPDEKTLFE	TLFEIVFQLLN	LNYFTGVFAFS	VGAATAGQTY	LPNDYVCKKGE
<i>B.taurus</i>	YQFPQSIDPLT	YMAFFEFNNRL	NGSYIRCYIWA	GGLPDERTLFE	TLFEIVFQGLN	LNYFTGVFAFS	VGAATAGQTY	LPNDYVCKKGE
<i>C.lupus</i>	YRFPQSIDPLT	YMAFFEFNSRL	NGSYIRCYIWA	GGLPDERTLFE	TLFEIVFQGLN	LNYFTGVFAFS	VGAATAGQTY	LPNDYVCKKGE
<i>G.gallus</i>	YQFPQSIDPLT	YLAFEFNNRL	NGSYIRCYIWA	GGLPDEKTLFE	TLFEIVFQLLN	LNYFTGVFAFS	VGAATAGQTY	LPNDFVCKKGE
<i>X.tropicalis</i>	LKFPQSIDPLT	YMAFFEFNNRL	NGSYIRCYIWA	GGLPDEDTLFE	TLFELVFQLLN	LNYFMGVFAFS	VGAATAGQTY	LPGDYVCKKGE
<i>D.rerio</i>	---	YNAFFEFNDRL	NGSYIRCYIFA	GGLPDETTVFE	TVFEIVFQLVN	VNYFVGVFAFS	IGAATAGEAY	LPNDFVCEKGE

**Table S4.** Conservation analysis of the novel canonical and non-canonical splice site variants on *CNGB1*, described in the study. This analysis was performed using the University of California Santa Cruz (UCSC) Genome Browser, available at <https://genome.ucsc.edu/index.html>. The interested residue is highlighted in red. Caps letters represent exons.

Nucleotide Genomic position (hg19)	58001027	57954451	57953001	57951166	57946900	57911751	57937725	57935346
cDNA Nucleotide position (NM_001297.4)	159+5	1644-3	1957+2	2166+6	2305-2	2492+2	2794+1	2893-7
Altered residue	t	c	c	g	c	c	t	t
H.sapiens	Ccactc <b>t</b> ccat	agggt <b>g</b> tcACC	TGGTc <b>a</b> ctcag	cactc <b>a</b> gtgtc	ggagg <b>t</b> cATGT	TGTCC <b>a</b> ctcgg	CGACC <b>a</b> ttct	agtgg <b>c</b> cctgt
P.troglodytes	Ccactc <b>t</b> ccat	agggt <b>g</b> tcGCC	TGGTc <b>a</b> ctcag	cactc <b>a</b> gtgtc	---	TGTCC <b>a</b> cttgg	CGACC <b>a</b> ttct	agtgg <b>c</b> cctgt
M.mulatta	Ccactc <b>t</b> ccac	agggt <b>g</b> tcGCC	TGGTc <b>a</b> ctcag	cactc <b>a</b> gtgtc	ggagg <b>t</b> cATGT	TGTCC <b>a</b> ctcgg	CGACC <b>a</b> ttct	agtga <b>c</b> cctgt
R.norvegicus	Ccactc <b>c</b> ccct	ggggt <b>g</b> tcACC	TGGTc <b>a</b> ctcaa	cattc <b>a</b> gtgtc	ggagg <b>t</b> cATGT	TGTCC <b>a</b> ctcgg	CGACC <b>a</b> ttct	gga---ccggt
B.taurus	Ccattc <b>t</b> tgac	aagg <b>t</b> tcACT	TGGTc <b>a</b> ctcag	cactc <b>a</b> gtgtc	ggagg <b>t</b> cATAT	TGTCC <b>a</b> ctcgg	CGACC <b>a</b> ttc-	agagc <b>c</b> cggt
C.lupus	Ccattc <b>t</b> ccga	cagg <b>g</b> ctACC	TGGTc <b>a</b> ctcag	cactc <b>a</b> gggcc	gaagg <b>t</b> cATGT	TGTCC <b>a</b> ctcgg	CGACC <b>a</b> ttc-	agaac <b>c</b> cctgt
G.gallus	---	-gggt <b>g</b> ctACG	TGGTc <b>a</b> ctct-	cactc <b>a</b> acctg-	ggagg <b>t</b> cATGG	TGTCC <b>a</b> -----	CGATC <b>a</b> ctct	aaac--ccggt
X.tropicalis	---	aggac <b>g</b> tcCCA	TGATc <b>a</b> ttca-	cattc <b>a</b> gt---	tacag <b>t</b> cATGT	TGTCC <b>a</b> ttc--	CGAAC <b>a</b> ttct	aga----cagt
D.rerio	---	aggac <b>g</b> -----	---	cactc <b>g</b> -----	--a-- <b>t</b> cATGT	TGTCC <b>a</b> ctcg-	CGACC <b>a</b> ttc-	-----gt

**Table S5.** Additional clinical phenotype of the subjects carrying likely disease-causing *CNGB1* variants included in the study. No data available for patients SRP480 and SRP629. BCVA: Best corrected visual acuity; OD: right eye; OS: left eye; OU: both eyes; wnl: within normal limits; ERM: epiretinal membrane; SW-FAF: Short-wavelength fundus autofluorescence; OCT: optical coherence tomography; n/a: not applicable.

ID	Age at visit (years)	BCVA (Snellen)		Visual field (degrees) (horizontal axis/vertical axis (isopter))				Color Vision (Axis affected)		SW-FAF		OCT	
		OD	OS	OD	OS	OU (III4)	Other comments	OD	OS	OD	OS	OD	OS
F5240 CIC09166	14	20/50	20/50	140/100 (V4)	140/100 (V4)	140/100	n/a	Tritan		Diffuse hypoautofluorescence in the far periphery with large ring of hyperautofluorescence outside the vascular arcade		Normal	
OPH2286	18	20/32	20/32	130/110 (V4)	130/120 (V4)	145/110	n/a	Not Available		Diffuse peripheral hypoautofluorescence with central area of preserved fluorescence surrounded by ring of hyperautofluorescence.		Reduction of the retinal thickness outside the center due to atrophy of the outer retinal layers; macular micro-cysts	
SRP541	29	20/25	20/20	Not Available									
ARRP278	30	20/32	20/25	20/20 (III4)	20/20 (III4)	Not available	n/a	Deutan		Diffuse peripheral hypoautofluorescence with central area of preserved fluorescence surrounded by ring of hyperautofluorescence		Reduction of the retinal thickness outside the center due to atrophy of the outer retinal layers, ERM	
TW8999826 <sup>#</sup>	30	20/20	20/20	Not Available						Diffuse peripheral hypoautofluorescence with central area of preserved fluorescence surrounded by ring of hyperautofluorescence		Reduction of the retinal thickness outside the center due to atrophy of the outer retinal layers	
TW20024045 <sup>#</sup>	31	20/20	20/20	Not Available						Diffuse peripheral hypoautofluorescence with central area of preserved fluorescence surrounded by ring of hyperautofluorescence		Reduction of the retinal thickness outside the center due to atrophy of the outer retinal layers	
SRP995	31	20/25	20/20	160/70 (III4) Complete annular	150/70 (III4) Large annular	Not available	n/a	wnl		Diffuse peripheral hypoautofluorescence with central area of preserved fluorescence surrounded by ring of hyperautofluorescence		Reduction of the retinal thickness outside the center due to atrophy of the outer retinal layers	

				scotoma between 20-40° nasally and 10-30° temporarily	scotoma between 20-40° nasally and 10-40° temporarily					
MRN:6822243	34	20/30	20/30	Not Available				Some hyper-autofluorescent lines in the inferior nasal retina are shown.	Normal	
OPH3784	36	20/20	20/25	Not available	145/115	n/a	Not available	Diffuse peripheral hypoautofluorescence with central area of preserved fluorescence surrounded by ring of hyperautofluorescence. RIF is large, outside the arcades.	Reduction of the retinal thickness outside the center due to atrophy of the outer retinal layers	
ARRP400	36	20/20	20/20	120/60 (III4)	130/120 (III4) elliptic area of scotoma between 30° and 40° inferiorly	Not available	n/a	wnl	Diffuse peripheral hypoautofluorescence with central area of preserved fluorescence surrounded by ring of hyperautofluorescence	Reduction of the retinal thickness outside the center due to atrophy of the outer retinal layers, ERM
F4300 CIC07722	39	20/25	20/32	Not Available						
SRP266	41	20/20	20/20	50/40 (III4) Some peripheral islands of	40/40 (III4) Some peripheral islands of	Not available	Some peripheral islands of residual vision in both eyes	wnl	Diffuse peripheral hypoautofluorescence with central area of preserved fluorescence surrounded by ring of hyperautofluorescence	Reduction of the retinal thickness outside the center due to atrophy of the outer retinal layers

				residual vision	residual vision							
ARRP349	41	20/80	20/100	10/10 (III4)	10/5 (III4)	Not available	n/a	Not available		Diffuse peripheral hypoautofluorescence with central area of hyperautofluorescence	Reduction of the retinal thickness outside the center due to atrophy of the outer retinal layers	
F141 CIC00189	43	20/320	20/250	150/110 (V4) Central scotoma	150/110 (V4) Central scotoma	160/110	Central scotoma	Tritan		Central area of hypoautofluorescence, surrounded by annular area of preserved fluorescence. Externally, starting from the main temporal vascular arcades, diffuse grainy peripheral hypoautofluorescence	Diffuse reduction of the retinal thickness due to the atrophy of the inner retinal layers. Diffuse disruption/atrophy of the ellipsoid zone, involving the fovea; intraretinal hyperreflective foci; traces of ERM (not involving the center)	
MEH28189	44	20/30	20/40	Not Available						Diffuse peripheral hypoautofluorescence with central area of preserved fluorescence surrounded by ring of hyperautofluorescence	Preservation of fovea in both eyes, with good preservation of central EZ	Preservation of fovea in both eyes, with good preservation of central EZ
F1107 CIC01530	45	20/63	20/32	20/20 (V4)	20/20 (V4) Some peripheral islands of residual vision	15/15	Some peripheral islands of residual vision in the left eye	wnl		Diffuse peripheral hypoautofluorescence with central area of preserved fluorescence surrounded by ring of hyperautofluorescence. Focal areas of hyperautofluorescence in the optic disc (drusen of the optic disc)	Central area of preserved retina, surrounded by area of atrophic ellipsoid zone and a more external area of RPE and inner retinal layer atrophy. ERM. Small intraretinal cysts (not involving the center)	
F3791 CIC06919	45	20/20	20/20	150/100 (V4)	150/110 (V4)	160/110	n/a	Tritan		Diffuse peripheral hypoautofluorescence with central area of preserved fluorescence surrounded by ring of hyperautofluorescence	Reduction of the retinal thickness outside the center due to atrophy of the outer retinal layers, ERM	
ARRP386	49	20/20	20/20	20/20 (III4)	20/20 (III4)	Not available	n/a	Not available		Diffuse peripheral hypoautofluorescence with central area of preserved fluorescence surrounded by ring of hyperautofluorescence	Reduction of the retinal thickness outside the center due to atrophy of the outer retinal layers, ERM	
ARRP398	49	20/20	20/20	Not interpretable	40/20 (III4)	Not available	n/a	wnl	Tritan	Diffuse peripheral hypoautofluorescence with central area of preserved	Reduction of the retinal thickness outside the center due to atrophy of the outer retinal layers, ERM	

										fluorescence surrounded by ring of hyperautofluorescence	
OPH1710	50	20/25	20/25	Not Available			145/105	n/a	wnl	Diffuse peripheral hypoautofluorescence with central area of preserved fluorescence surrounded by ring of hyperautofluorescence. RIF is inside the arcades. Some peripheral punched-out round hypoAF lesions.	Reduction of the retinal thickness outside the center due to atrophy of the outer retinal layers; macular micro-cysts
MRN:8759303	50	20/100	20/30	Not Available							
F463 CIC00691*	51	20/125	20/50	30/20 (V4)	30/20 (V4)	30/20	n/a	Deutan	Diffuse peripheral hypoautofluorescence with central area of preserved fluorescence surrounded by ring of hyperautofluorescence	Central area of preserved retina, surrounded by area of atrophic ellipsoid zone.	
F463 CIC02695*	51	20/50	20/20	30/30 (V4)	30/40 (V4)	40/40	n/a	wnl	Diffuse peripheral hypoautofluorescence with central area of preserved fluorescence surrounded by ring of hyperautofluorescence	Central area of preserved retina, surrounded by area of atrophic ellipsoid zone; traces of ERM (not involving the center)	
F2070 CIC04317	51	20/20	20/32	20/20 (V4) Some peripheral islands of residual vision	20/20 (V4) Some peripheral islands of residual vision	20/20	Some peripheral islands of residual vision in both eyes	wnl	Diffuse peripheral hypoautofluorescence with central area of preserved fluorescence surrounded by ring of hyperautofluorescence	Central area of preserved retina, surrounded by area of atrophic ellipsoid zone and a more external area (nasally) of RPE and inner retinal layer atrophy.	
F5462 CIC09504	52	20/125	20/80	Not available				Deutan	Diffuse peripheral hypoautofluorescence with central area of preserved fluorescence surrounded by ring of hyperautofluorescence	Reduction of the retinal thickness outside the center due to atrophy of the outer retinal layers	



F4053 CIC07355	55	20/25	20/20	40/20 (V4)	40/20 (V4)	40/20	n/a	Tetartan	Diffuse peripheral hypoautofluorescence with central area of preserved fluorescence surrounded by ring of hyperautofluorescence	Central area of preserved retina, surrounded by area of atrophic ellipsoid zone. Intraretinal hyperreflective foci and some intraretinal cysts (not involving the center)	
F5830 CIC10130	56	20/32	20/32	10/10 (V4)	10/10 (V4)	15/15	n/a	wnl	Diffuse peripheral hypoautofluorescence with central area of preserved fluorescence surrounded by ring of hyperautofluorescence	Central area of preserved retina, surrounded by area of atrophic ellipsoid zone. some intraretinal cysts (not involving the center); traces of ERM in the left eye (not involving the center)	
ARRP396	58	20/40	20/63	5/5 (III4)	5/5 (III4)	Not available	n/a	Not available	Diffuse peripheral hypoautofluorescence with small central area of preserved fluorescence	Reduction of the retinal thickness outside the center due to atrophy of the outer retinal layers, tubulations, ERM	
F3038 CIC05823	64	Hands motion	20/160	-	5/5 (V4)	5/5	Some residual islands of light perception in the right eye	Unreliable	Central area of hypoautofluorescence, surrounded by thin annular area of preserved fluorescence. More external diffuse grainy hypoautofluorescence	Diffuse reduction of the retinal thickness due to the atrophy of the inner retinal layers. Diffuse disruption/atrophy of the ellipsoid zone, involving the fovea; intraretinal hyperreflective foci	
MRN:1203567 687	72	No light perception	No light perception	Not Available				Generalized hypoautofluorescence	Diffuse retinal thinning with outer retinal atrophy		
MEH16550	73	20/30	No Light Perception	Not available				Diffuse peripheral hypoautofluorescence with central area of preserved fluorescence surrounded by ring of hyperautofluorescence.	Impossible to perform	Reduction of the retinal thickness outside the center due to atrophy of the outer retinal layers	Impossible to perform

F4517 CIC08096	77	20/10 0	20/12 5	5/5 (V4)	5/5 (V4)	10/1 0	-	Tritan	Diffuse peripheral hypoautofluorescence with small central area of preserved fluorescence	Reduction of the retinal thickness outside the center due to atrophy of the outer retinal layers
SRP480	Not Available									
SRP629	Not Available									

\* and # : Subjects are siblings

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