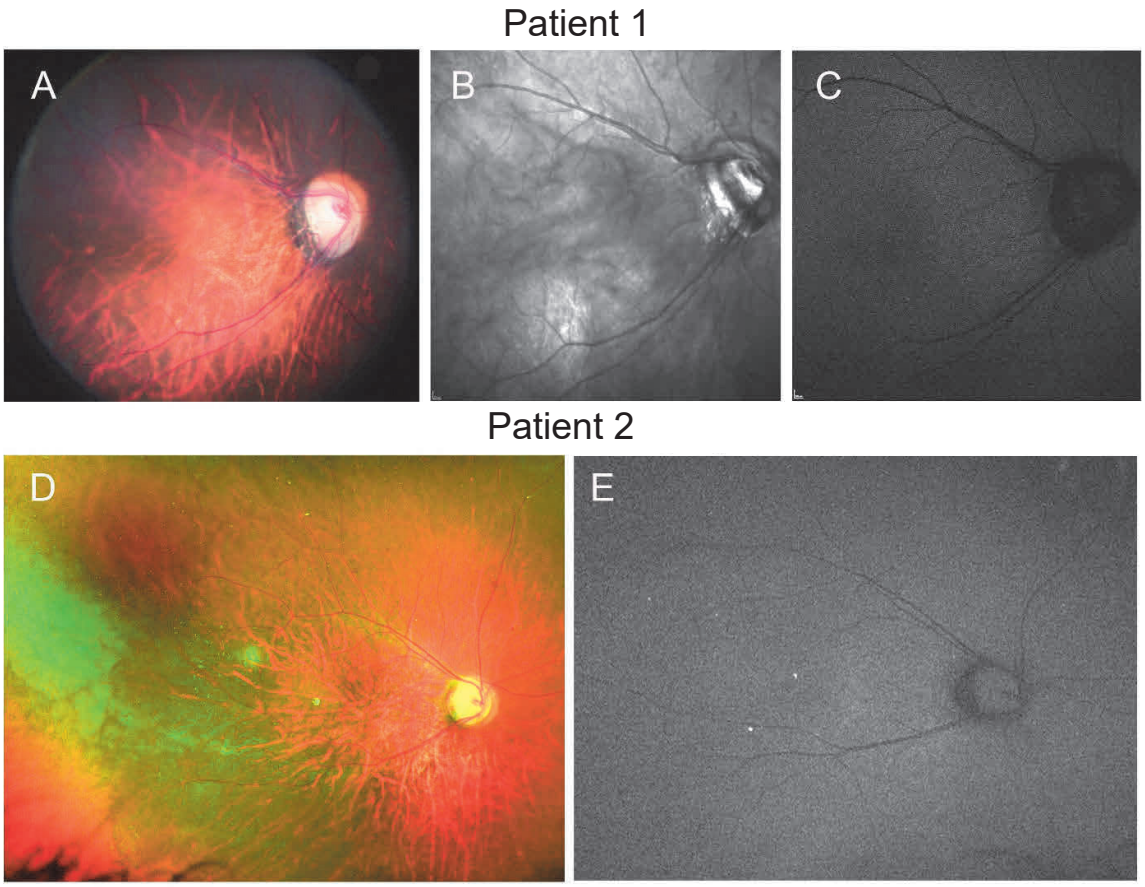
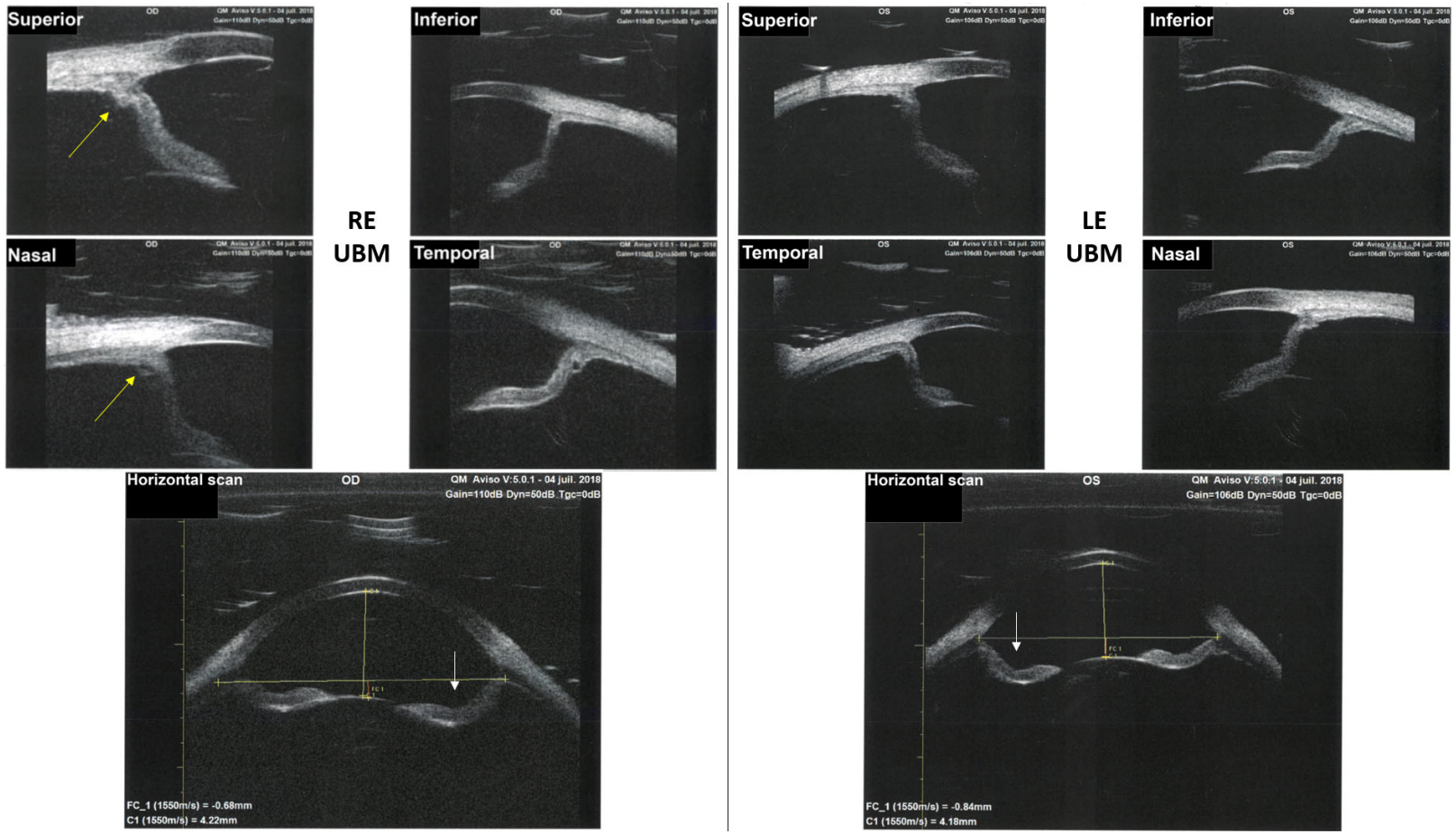
Supplemental Online Content

Smirnov VM, Robert MP, Condroyer C, et al. Association of missense variants in *VSX2* with a peculiar form of congenital stationary night blindness affecting all bipolar cells. *JAMA Ophthamol*. Published online October 20, 2022. doi:10.1001/jamaophthalmol.2022.4146

This supplemental material has been provided by the authors to give readers additional information about their work.



eFigure 1. Multimodal retinal imaging in patients 1 and 2 from the same family. Top, patient 1. *A, fundus photo. Myopic fundus abnormalities with oval tilted optic discs, temporal pallor and peripapillary chorio-retinal atrophy, narrowed retinal vessels and thinned retina with increased choroidal visibility. B, Infrared reflectance. No obvious changes in retinal reflectance besides increased choroidal visibility. C, Short-wavelength fundus autofluorescence. No obvious changes.* ***Bottom, patient 2.*** *D, wide-field fundus photo. Myopic fundus abnormalities with oval titled optic disc, temporal pallor, narrowed retinal vessels, retinal thinning. White-without-pressure in temporal periphery. E, wide-field short-wavelength fundus autofluorescence. No obvious changes.*



eFigure 2. Ultrasound biomicroscopy in patient 3. *Hypoplastic ciliary body (yellow arrows). Posterior iris bowing (white arrows).*

eTable 1. The molecular diagnosis NGS panel including 164 genes associated with pediatric inherited retinal diseases.

Name	Transcript	Chr	Start(hg19)	End(hg19)	Refseq	Description
ABCA4	ENST00000370225_1	1	94458393	94586688	NM_000350	ATP-binding cassette, sub-family A (ABC1), member 4
ACBD5	ENST00000396271_10	10	27484146	27529744	NM_145698	acyl-CoA binding domain containing 5
ADAM9	ENST00000487273_8	8	38854505	38962520	NM_003816	ADAM metallopeptidase domain 9
AHI1	ENST00000327035_6	6	135708922	135818883	NM_001134832	Abelson helper integration site 1
	ENST00000457866_6	6	135605124	135818903	NM_017651	Abelson helper integration site 1
AIPL1	ENST00000381129_17	17	6327057	6338505	NM_014336	aryl hydrocarbon receptor interacting protein-like 1
ALMS1	ENST00000264448_2	2	73612886	73837046	XM_005264552	Alstrom syndrome 1
ARL13B	ENST00000471138_3	3	93698999	93772913	NM_182896	ADP-ribosylation factor-like 13B
ARL2BP	ENST00000219204_16	16	57279010	57287516	NM_012106	ADP-ribosylation factor-like 2 binding protein
ARL6	ENST00000493990_3	3	97483365	97519953		ADP-ribosylation factor-like 6
ATF6	ENST00000367942_1	1	161736084	161933860	NM_007348	activating transcription factor 6
ATXN7	ENST00000484332_3	3	63953420	63985472	NM_001128149	ataxin 7
	ENST00000538065_3	3	63898275	63989129		ataxin 7
C1QTNF5	ENST00000528368_11	11	119209652	119211593	NM_001278431	C1q and tumor necrosis factor related protein 5
C21orf2	ENST00000397956_21	21	45749774	45759276	NM_001271441	chromosome 21 open reading frame 2
C2orf71	ENST00000331664_2	2	29284558	29297127	NM_001029883	chromosome 2 open reading frame 71
C5orf42	ENST00000425232_5	5	37106330	37249530	XM_005248352	chromosome 5 open reading frame 42
C8orf37	ENST00000286688_8	8	96257147	96281429	NM_177965	chromosome 8 open reading frame 37
CA4	ENST00000300900_17	17	58227297	58236901	NM_000717	carbonic anhydrase IV
CABP4	ENST00000438189_11	11	67219886	67226699	XM_005274116	calcium binding protein 4
	ENST00000325656_11	11	67222818	67226524	XM_005274114	calcium binding protein 4
CACNA1F	ENST00000376265_X	X	49061523	49089833	NM_005183	calcium channel, voltage-dependent, L type, alpha 1F subunit
	ENST00000376251_X	X	49061523	49089771	NM_001256790	calcium channel, voltage-dependent, L type, alpha 1F subunit
CACNA2D4	ENST00000382722_12	12	1901123	2028002	NM_172364	calcium channel, voltage-dependent, alpha 2/delta subunit 4
CC2D2A	ENST00000503658_4	4	15471637	15483000		coiled-coil and C2 domain containing 2A
	ENST00000515124_4	4	15471536	15483883	NM_001164720	coiled-coil and C2 domain containing 2A
	ENST00000413206_4	4	15471489	15603180	XM_005248179	coiled-coil and C2 domain containing 2A
CCT2	ENST00000299300_12	12	69979114	69995350	XM_005268574	chaperonin containing TCP1, subunit 2 (beta)

CDH3	ENST00000264012_16	16	68678739	68732971	NM_001793	cadherin 3, type 1, P-cadherin (placental)
CDHR1	ENST00000332904_10	10	85954410	85979377	NM_001171971	cadherin-related family member 1
	ENST00000372117_10	10	85954414	85977122	NM_033100	cadherin-related family member 1
CEP104	ENST00000378230_1	1	3728645	3773763	XM_005244815	centrosomal protein 104kDa
CEP164	ENST00000278935_11	11	117198571	117283984	XM_005271460	centrosomal protein 164kDa
CEP290	ENST00000552810_12	12	88442797	88535993	XM_005269161	centrosomal protein 290kDa
CEP41	ENST00000489512_7	7	130058875	130080897	NM_001257160	centrosomal protein 41kDa
	ENST00000223208_7	7	130033612	130081078	XM_005277633	centrosomal protein 41kDa
CERKL	ENST00000339098_2	2	182402911	182521733		ceramide kinase-like
CLN3	ENST00000359984_16	16	28488600	28503403	NM_000086	ceroid-lipofuscinosis, neuronal 3
CLRN1	ENST00000328863_3	3	150645723	150690495	NM_001195794	clarin 1
	ENST00000295911_3	3	150643950	150662023	NM_052995	clarin 1
CLUAP1	ENST00000576634_16	16	3550924	3589048	NM_015041	clusterin associated protein 1
CNGA1	ENST00000402813_4	4	47937994	47983552	XM_005248050	cyclic nucleotide gated channel alpha 1
CNGA3	ENST00000393504_2	2	98962618	99015057	NM_001298	cyclic nucleotide gated channel alpha 3
CNGB1	ENST00000311183_16	16	57988579	58005020	NM_001135639	cyclic nucleotide gated channel beta 1
	ENST00000251102_16	16	57917706	58005016	NM_001297	cyclic nucleotide gated channel beta 1
CNGB3	ENST00000320005_8	8	87586163	87755903	NM_019098	cyclic nucleotide gated channel beta 3
CNNM4	ENST00000377075_2	2	97426639	97477628	NM_020184	cyclin M4
COL18A1	ENST00000400337_21	21	46825052	46933634	XM_005261181	collagen, type XVIII, alpha 1
	ENST00000355480_21	21	46875403	46933634	XM_005261178	collagen, type XVIII, alpha 1
	ENST00000359759_21	21	46875424	46933633	XM_005261182	collagen, type XVIII, alpha 1
CRB1	ENST00000535699_1	1	197170592	197447212	NM_001257965	crumbs homolog 1 (Drosophila)
	ENST00000367400_1	1	197237408	197447585	NM_201253	crumbs homolog 1 (Drosophila)
CRX	ENST00000221996_19	19	48325097	48346587	NM_000554	cone-rod homeobox
CSPP1	ENST00000262210_8	8	67976603	68108498	XM_005251311	centrosome and spindle pole associated protein 1
CYP4V2	ENST00000378802_4	4	187112674	187131955	XM_005262935	cytochrome P450, family 4, subfamily V, polypeptide 2
DHDDS	ENST00000360009_1	1	26758846	26797785	NM_024887	dehydrodolichyl diphosphate synthase
DHX38	ENST00000268482_16	16	72127461	72146811	XM_005256268	DEAH (Asp-Glu-Ala-His) box polypeptide 38
DRAM2	ENST00000539140_1	1	111659957	111682838	NM_178454	DNA-damage regulated autophagy modulator 2
EFEMP1	ENST00000394555_2	2	56093102	56151274	NM_001039348	EGF containing fibulin-like extracellular matrix protein 1
ELOVL4	ENST00000369816_6	6	80624529	80657297	NM_022726	ELOVL fatty acid elongase 4
EYS	ENST00000370621_6	6	64430032	66417107		eyes shut homolog (Drosophila)

	ENST00000393380_6	6	66039165	66417118	NM_001142801	eyes shut homolog (Drosophila)
FAM161A	ENST00000404929_2	2	62051991	62081188	NM_001201543	family with sequence similarity 161, member A
FLVCR1	ENST00000366971_1	1	213031597	213072705	NM_014053	feline leukemia virus subgroup C cellular receptor 1
FSCN2	ENST00000334850_17	17	79495558	79504106	XM_005257195	fascin homolog 2, actin-bundling protein, retinal (Strongylocentrotus purpuratus)
GNAT1	ENST00000232461_3	3	50229045	50233949	NM_144499	guanine nucleotide binding protein, alpha transducing activity polypeptide 1
GNAT2	ENST00000351050_1	1	110145889	110155679	NM_005272	guanine nucleotide binding protein , alpha transducing activity polypeptide 2
GNPTG	ENST00000204679_16	16	1401924	1413352	NM_032520	N-acetylglucosamine-1-phosphate transferase, gamma subunit
GPR125	ENST00000334304_4	4	22389007	22517677	XM_005248137	G protein-coupled receptor 125
GPR179	ENST00000342292_17	17	36481493	36499693	NM_001004334	G protein-coupled receptor 179
GRM6	ENST00000231188_5	5	178405328	178422124	NM_000843	glutamate receptor, metabotropic 6
GUCA1A	ENST00000053469_6	6	42123174	42147794	XM_005249037	guanylate cyclase activator 1A (retina)
GUCA1B	ENST00000230361_6	6	42152139	42162654	NM_002098	guanylate cyclase activator 1B (retina)
GUCY2D	ENST00000254854_17	17	7905912	7923657	NM_000180	guanylate cyclase 2D, membrane (retina-specific)
HGSNAT	ENST00000379644_8	8	42995598	43057998	XM_005273692	heparan-alpha-glucosaminide N-acetyltransferase
HK1	ENST00000404387_10	10	71048500	71160891	XM_005269736	hexokinase 1
	ENST00000359426_10	10	71078600	71161638	XM_005269737	hexokinase 1
	ENST00000360289_10	10	71029756	71161635	NM_033498	hexokinase 1
	ENST00000298649_10	10	71075610	71161635	NM_033496	hexokinase 1
IDH3B	ENST00000380851_20	20	2639041	2644865	NM_001258384	isocitrate dehydrogenase 3 (NAD+) beta
	ENST00000380843_20	20	2639041	2644865	XM_005260716	isocitrate dehydrogenase 3 (NAD+) beta
IFT140	ENST00000426508_16	16	1560428	1662111	XM_005255724	intraflagellar transport 140 homolog (Chlamydomonas)
IFT172	ENST00000260570_2	2	27667238	27712624	NM_015662	intraflagellar transport 172 homolog (Chlamydomonas)
IMPDH1	ENST00000338791_7	7	128032331	128050306	XM_005250315	IMP (inosine 5'-monophosphate) dehydrogenase 1
	ENST00000354269_7	7	128032332	128050036	XM_005250315	IMP (inosine 5'-monophosphate) dehydrogenase 1
IMPG1	ENST00000369950_6	6	76630832	76782395	NM_001563	interphotoreceptor matrix proteoglycan 1
IMPG2	ENST00000193391_3	3	100941390	101039404	NM_016247	interphotoreceptor matrix proteoglycan 2
INPP5E	ENST00000371712_9	9	139323071	139334274	XM_005266094	inositol polyphosphate-5-phosphatase, 72 kDa
INVS	ENST00000262457_9	9	102861538	103063282	NM_014425	inversin
IQCB1	ENST00000310864_3	3	121488610	121553926	XM_005247913	IQ motif containing B1
ITM2B	ENST00000378565_13	13	48807294	48836460	NM_021999	integral membrane protein 2B

KCNJ13	ENST00000233826_2	2	233631174	233641278	NM_002242	potassium inwardly-rectifying channel, subfamily J, member 13
KCNV2	ENST00000382082_9	9	2717502	2730037	NM_133497	potassium channel, subfamily V, member 2
KIAA1549	ENST00000422774_7	7	138522270	138666064		KIAA1549
KIF7	ENST00000394412_15	15	90171208	90198682	XM_005254904	kinesin family member 7
KIZ	ENST00000619189_20	20	21106695	21227260	XM_011529298	kizuna centrosomal protein
KLHL7	ENST00000322275_7	7	23145404	23165664	NM_001172428	kelch-like family member 7
	ENST00000339077_7	7	23145403	23217533	NM_001031710	kelch-like family member 7
LAMA1	ENST00000389658_18	18	6941743	7117813	NM_005559	laminin, alpha 1
LRAT	ENST00000336356_4	4	155665123	155674270	NM_004744	lecithin retinol acyltransferase (phosphatidylcholine--retinol O-acyltransferase)
LRIT3	ENST00000594814_4	4	110769358	110793471	NM_198506	leucine-rich repeat, immunoglobulin-like and transmembrane domains 3
MAK	ENST00000474039_6	6	10762956	10838764	XM_005249114	male germ cell-associated kinase
MERTK	ENST00000295408_2	2	112656056	112787138	XM_005263568	c-mer proto-oncogene tyrosine kinase
NEK2	ENST00000366998_1	1	211839772	211848899	NM_001204183	NIMA-related kinase 2
	ENST00000366999_1	1	211836114	211848960	NM_002497	NIMA-related kinase 2
NEUROD1	ENST00000295108_2	2	182541194	182545603	NM_002500	neuronal differentiation 1
NMNAT1	ENST00000377205_1	1	10003486	10045556	NM_022787	nicotinamide nucleotide adenylyltransferase 1
	ENST00000403197_1	1	10003486	10041824	XM_005263489	nicotinamide nucleotide adenylyltransferase 1
NPHP1	ENST00000316534_2	2	110879888	110962619		nephronophthisis 1 (juvenile)
NPHP3	ENST00000337331_3	3	132400472	132441286	NM_153240	nephronophthisis 3 (adolescent)
NPHP4	ENST00000378156_1	1	5922878	6052531	XM_005263447	nephronophthisis 4
NR2E3	ENST00000621098_15	15	72102932	72107270	NM_016346	nuclear receptor subfamily 2 group E member 3
NRL	ENST00000397002_14	14	24549316	24553834	XM_005267709	neural retina leucine zipper
NYX	ENST00000342595_X	X	41306687	41334963	NM_022567	nyctalopin
OFD1	ENST00000340096_X	X	13752864	13787472	XM_005274601	oral-facial-digital syndrome 1
OPN1LW	ENST00000369951_X	X	153409698	153424507	NM_020061	opsin 1 (cone pigments), long-wave-sensitive
OPN1MW	ENST00000369935_X	X	153448107	153461633	NM_000513	opsin 1 (cone pigments), medium-wave-sensitive
OPN1SW	ENST00000249389_7	7	128412545	128415844	NM_001708	opsin 1 (cone pigments), short-wave-sensitive
OR2W3	ENST00000537741_1	1	248031277	248060449		olfactory receptor, family 2, subfamily W, member 3
OTX2	ENST00000339475_14	14	57267425	57277187	NM_001270524	orthodenticle homeobox 2
PAX2	ENST00000428433_10	10	102505468	102589698	XM_005269873	paired box 2
	ENST00000361791_10	10	102505468	102589074	NM_003988	paired box 2

PCYT1A	ENST00000292823_3	3	195961239	196014584	XM_005269343	phosphate cytidylyltransferase 1, choline, alpha
PDE6A	ENST00000255266_5	5	149237519	149324356	NM_000440	phosphodiesterase 6A, cGMP-specific, rod, alpha
PDE6B	ENST00000496514_4	4	619395	664542		phosphodiesterase 6B, cGMP-specific, rod, beta
PDE6C	ENST00000371447_10	10	95372345	95425767	NM_006204	phosphodiesterase 6C, cGMP-specific, cone, alpha prime
PDE6G	ENST00000331056_17	17	79617489	79623607	NM_002602	phosphodiesterase 6G, cGMP-specific, rod, gamma
PDE6H	ENST00000266395_12	12	15125956	15134799	NM_006205	phosphodiesterase 6H, cGMP-specific, cone, gamma
PITPNM3	ENST00000262483_17	17	6354585	6459814	NM_031220	PITPNM family member 3
POC1B	ENST00000313546_12	12	89813495	89919801	NM_172240	POC1 centriolar protein B
PPT1	ENST00000433473_1	1	40538379	40563375	NM_000310	palmitoyl-protein thioesterase 1
PRCD	ENST00000586148_17	17	74536172	74539469		progressive rod-cone degeneration
PROM1	ENST00000447510_4	4	15969849	16077741	NM_006017	prominin 1
PRPF3	ENST00000324862_1	1	150293925	150325671	NM_004698	pre-mRNA processing factor 3
PRPF31	ENST00000321030_19	19	54618837	54635140	NM_015629	pre-mRNA processing factor 31
PRPF4	ENST00000374198_9	9	116037922	116055056	NM_001244926	pre-mRNA processing factor 4
PRPF6	ENST00000266079_20	20	62612488	62664453	NM_012469	pre-mRNA processing factor 6
PRPF8	ENST00000304992_17	17	1553923	1588176	NM_006445	pre-mRNA processing factor 8
PRPH2	ENST00000230381_6	6	42664340	42690312	NM_000322	peripherin 2 (retinal degeneration, slow)
RAB28	ENST00000330852_4	4	13369348	13485989	NM_001017979	RAB28, member RAS oncogene family
	ENST00000288723_4	4	13369348	13485989	NM_004249	RAB28, member RAS oncogene family
	ENST00000338176_4	4	13369349	13485989	XM_005248217	RAB28, member RAS oncogene family
RASSF8	ENST00000381352_12	12	26111962	26232825	XM_005253295	Ras association (RalGDS/AF-6) domain family (N-terminal) member 8
	ENST00000542865_12	12	26126688	26222418	NM_001164747	Ras association (RalGDS/AF-6) domain family (N-terminal) member 8
RAX2	ENST00000555978_19	19	3769087	3772209	NM_032753	retina and anterior neural fold homeobox 2
RBP3	ENST00000224600_10	10	48381487	48390991	NM_002900	retinol binding protein 3, interstitial
RBP4	ENST00000371464_10	10	95351444	95360983	NM_006744	retinol binding protein 4, plasma
RD3	ENST00000367002_1	1	211649864	211666259	NM_001164688	retinal degeneration 3
RDH11	ENST00000381346_14	14	68143518	68162531	XM_005267732	retinol dehydrogenase 11 (all-trans/9-cis/11-cis)
RDH12	ENST00000551171_14	14	68168603	68201169	NM_152443	retinol dehydrogenase 12 (all-trans/9-cis/11-cis)
RDH5	ENST00000257895_12	12	56114182	56118489	NM_001199771	retinol dehydrogenase 5 (11-cis/9-cis)
RGR	ENST00000359452_10	10	86004809	86019716	NM_002921	retinal G protein coupled receptor
RHO	ENST00000296271_3	3	129247483	129254012	NM_000539	rhodopsin
RIMS1	ENST00000521978_6	6	72596727	73110416	NM_014989	regulating synaptic membrane exocytosis 1

	ENST00000517827_6	6	72926463	73110571	NM_001168410	regulating synaptic membrane exocytosis 1
	ENST00000401910_6	6	72922514	73110607	NM_001168407	regulating synaptic membrane exocytosis 1
RLBP1	ENST00000268125_15	15	89753100	89764982	NM_000326	retinaldehyde binding protein 1
ROM1	ENST00000278833_11	11	62380213	62382592	NM_000327	retinal outer segment membrane protein 1
RP1	ENST00000220676_8	8	55528627	55543394	NM_006269	retinitis pigmentosa 1 (autosomal dominant)
RP2	ENST00000218340_X	X	46696375	46741793	NM_006915	retinitis pigmentosa 2 (X-linked recessive)
RP9	ENST00000297157_7	7	33134409	33149002	NM_203288	retinitis pigmentosa 9 (autosomal dominant)
RPE65	ENST00000262340_1	1	68894505	68915642	NM_000329	retinal pigment epithelium-specific protein 65kDa
RPGR	ENST00000378505_X	X	38143662	38186797	NM_001034853	retinitis pigmentosa GTPase regulator
	ENST00000318842_X	X	38128416	38186817	NM_000328	retinitis pigmentosa GTPase regulator
RPGRIP1	ENST00000400017_14	14	21756136	21819454	XM_005267881	retinitis pigmentosa GTPase regulator interacting protein 1
RPGRIP1L	ENST00000379925_16	16	53634690	53737758	NM_015272	RPGRIP1-like
SAG	ENST00000409110_2	2	234216467	234255701	XM_005246099	S-antigen; retina and pineal gland (arrestin)
SDCCAG8	ENST00000366541_1	1	243419358	243663394	XM_005273016	serologically defined colon cancer antigen 8
SEMA4A	ENST00000368285_1	1	156123318	156147535	XM_005245441	semaphorin 4A
SLC24A1	ENST00000537259_15	15	65903743	65953333		solute carrier family 24 (sodium/potassium/calcium exchanger), member 1
	ENST00000261892_15	15	65914270	65948598	XM_005254778	solute carrier family 24 (sodium/potassium/calcium exchanger), member 1
SLC7A14	ENST00000231706_3	3	170177372	170303863	NM_020949	solute carrier family 7, member 14
SNRNP200	ENST00000323853_2	2	96940074	96971253	NM_014014	small nuclear ribonucleoprotein 200kDa (U5)
SPATA7	ENST00000393545_14	14	88851874	88904800	XM_005267857	spermatogenesis associated 7
TIMP3	ENST00000266085_22	22	33197687	33259030	NM_000362	TIMP metallopeptidase inhibitor 3
TMEM138	ENST00000278826_11	11	61129473	61136981	NM_016464	transmembrane protein 138
TMEM216	ENST00000334888_11	11	61159832	61166335	XM_005274039	transmembrane protein 216
TMEM237	ENST00000409883_2	2	202484907	202508240	XM_005246785	transmembrane protein 237
	ENST00000409444_2	2	202484907	202507667	NM_152388	transmembrane protein 237
TOPORS	ENST00000360538_9	9	32540542	32552551	NM_005802	topoisomerase I binding, arginine/serine-rich, E3 ubiquitin protein ligase
TPP1	ENST00000299427_11	11	6634000	6640692	NM_000391	tripeptidyl peptidase I
TRPM1	ENST00000559179_15	15	31361579	31393930	NM_001252030	transient receptor potential cation channel, subfamily M, member 1
	ENST00000256552_15	15	31293537	31393924	NM_001252024	transient receptor potential cation channel, subfamily M, member 1

	ENST00000542188_15	15	31293553	31453476	NM_001252020	transient receptor potential cation channel, subfamily M, member 1
TTC8	ENST00000380656_14	14	89291006	89344331	NM_144596	tetratricopeptide repeat domain 8
	ENST00000338104_14	14	89291000	89344332	XM_005267337	tetratricopeptide repeat domain 8
TTLL5	ENST00000298832_14	14	76127621	76421421	XM_005267450	tubulin tyrosine ligase-like family, member 5
TTPA	ENST00000260116_8	8	63972342	63998612	NM_000370	tocopherol (alpha) transfer protein
TUB	ENST00000299506_11	11	8102909	8123515	NM_177972	tubby bipartite transcription factor
TUB	ENST00000305253_11	11	8060180	8127659	XM_005253109	tubby bipartite transcription factor
TULP1	ENST00000229771_6	6	35465651	35480715	NM_003322	tubby like protein 1
UNC119	ENST00000301032_17	17	26873726	26879649	NM_054035	unc-119 homolog (C. elegans)
	ENST00000335765_17	17	26873725	26879686	XM_005258066	unc-119 homolog (C. elegans)
USH2A	ENST00000366942_1	1	216347288	216596738	NM_007123	Usher syndrome 2A (autosomal recessive, mild)
	ENST00000307340_1	1	215796236	216596738	NM_206933	Usher syndrome 2A (autosomal recessive, mild)
VPS13B	ENST00000355155_8	8	100025494	100222015	NM_015243	vacuolar protein sorting 13 homolog B (yeast)
	ENST00000358544_8	8	100025494	100889808	XM_005250803	vacuolar protein sorting 13 homolog B (yeast)
WDR19	ENST00000399820_4	4	39184024	39287430	XM_005262658	WD repeat domain 19
ZNF408	ENST00000311764_11	11	46722368	46727462	NM_024741	zinc finger protein 408
ZNF423	ENST00000561648_16	16	49521435	49856650	XM_005255857	zinc finger protein 423
ZNF513	ENST00000323703_2	2	27600098	27603592	XM_005264143	zinc finger protein 513

eTable2. Homozygous variants found in ES for autosomal recessive model (MAF<0.05).

Gene	gDNA change (hg19)	cDNA change (Transcript Number)	amino acid change
ITIH2	Chr10: 7769692	c.1180C>T (NM_002216.2)	p.(Arg394Trp)
PRDM10	Chr11: 129800931	c.1510C>T (NM_020228.2)	p.(Arg504Cys)
VSX2	Chr14: 74726320	c.595C>T (NM_182894.2)	p.(Arg199Cys)
BCR	Chr22: 23656782	c.3607C>G (NM_004327.3)	p.(Leu1203Val)

eAppendix. Discussion of *VSX2* variants identified herein in respect to the literature

Iseri et al. reported a consanguineous Iranian pedigree of two siblings with microphthalmia and coloboma homozygous for the c.249delG p.(Leu84Serfs*57) pathogenic variant in *VSX2*[1]. The siblings were blind with undetectable ffERG responses. Their heterozygous parents presented a significant reduction of ffERG a- and b-waves under both dark- and light-adapted conditions with an additional reduction in the b/a amplitude ratio to a bright flash under dark-adapted conditions. Authors hypothesized that this *VSX2* gene defects might act as semi-dominant and produce a generalized retinal dysfunction affecting rod and cone systems with an additional post-phototransduction dysfunction while in heterozygous state. Khan et al. reported a female patient homozygous for the c.773delA p.(Lys258Serfs*44) variant in *VSX2* and a clinical phenotype close to Knobloch syndrome: infantile upbeat nystagmus, high myopia, low BCVA, atrophic chorio-retinal changes and lens luxation[2]. ffERG found delayed and decreased scotopic and photopic responses, with photopic responses being more severely altered. However, there was no indication of an electronegative ERG response. Nevertheless, the clinical picture of the latter subject resembles best the phenotype of the subjects presented herein.

Moreover, the clinical phenotype of our patients was more complex than known CSNB phenotypes. It included developmental abnormalities as anterior segment abnormalities (lens subluxation and cataracts in patients 1 and 3), ciliary body hypoplasia in patient 3, atrophic peripheral retinal changes (patients 1 and 2) and wedge-shaped inferior chorio-retinal atrophy reminiscent of chorio-retinal coloboma and foveal hypoplasia in patient 3. Noteworthy, the

latter patient was myopic in spite of the short axial length (Table 1 in the main article) that is suggestive of index myopia most probably due to anterior segment abnormalities. The ocular disease thus could be more properly characterized as ocular developmental abnormality and retinopathy with a bipolar-specific phenotype. Nevertheless, the initial presentation in the youngest patient was very close to CSNB, anterior segment abnormalities appearing probably later in life. In addition, we need to wait for a longer follow-up to assess the non-progressive character of retinal involvement of patient 3.

eReferences

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2. Khan AO, Aldahmesh MA, Noor J, Salem A, Alkuraya FS. Lens Subluxation and Retinal Dysfunction in a Girl with Homozygous VSX2 Mutation. *Ophthalmic Genetics*. 2015;36(1):8-13. doi:10.3109/13816810.2013.827217