SUPPORTING INFORMATION

Supp. Figure S1. Pedigrees of sporadic and familial cases examined in this study

Supp. Figure S2. Pedigrees with variants and Sanger sequencing results

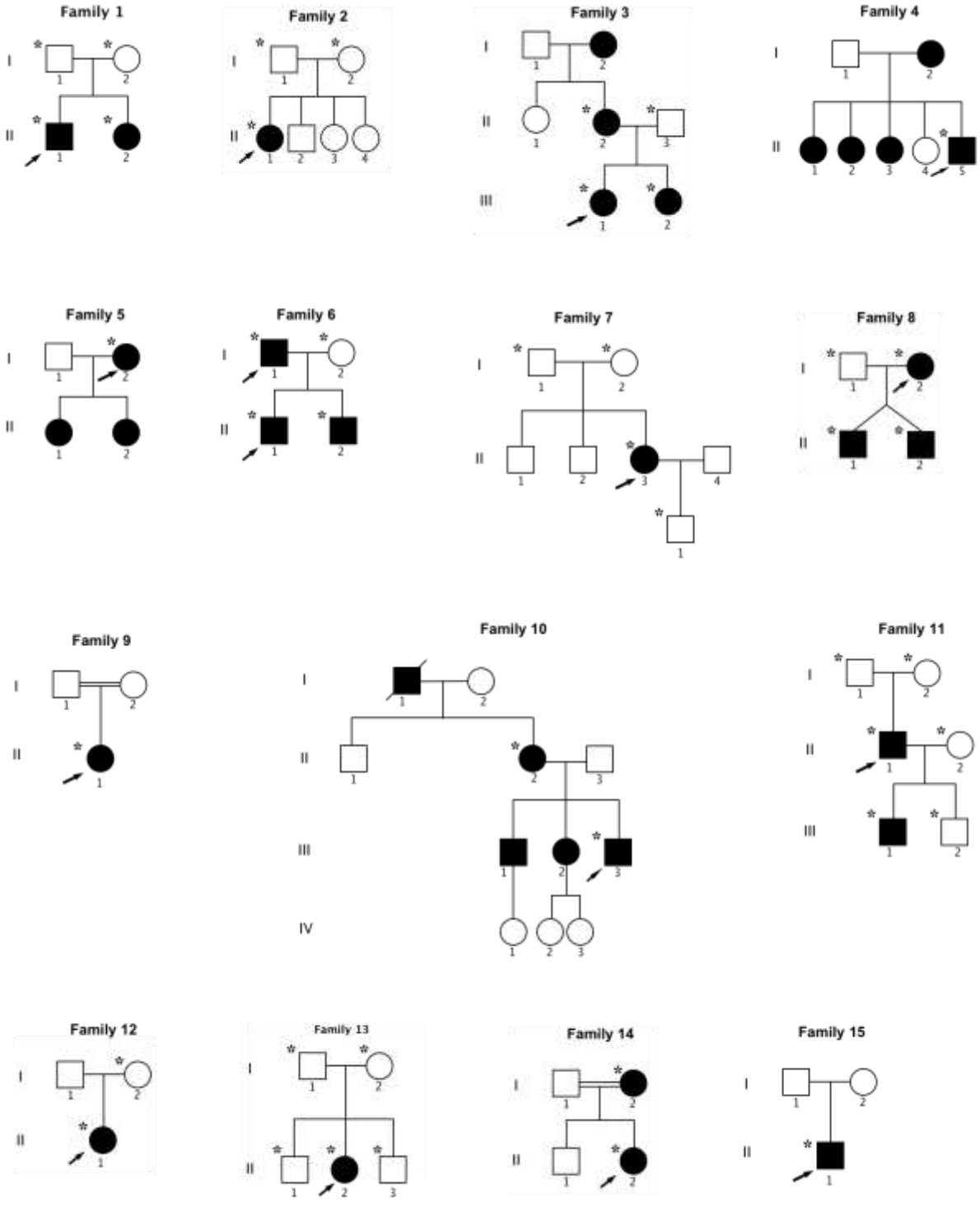
Supp. Table S1. Clinical features in 46 families with sporadic and familial cataracts

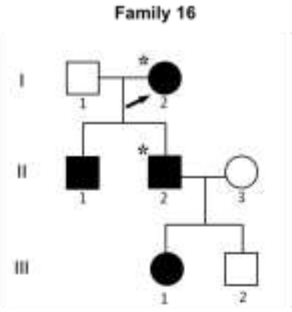
Supp. Table S2. List of Cataract Genes

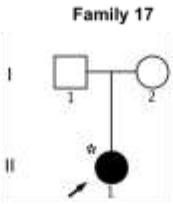
Supp. Tables S3 A-D.
3A. & 3B. NGS analysis and variant prioritization for TruSeq (A) and TruSight (B)
3C. & 3D. Gaps on the TruSeq (C) and TruSight (D) platforms

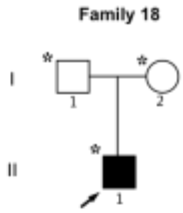
Supp. Table S4. Families with likely non-causative variants

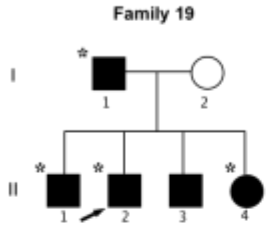
Supp. Figure S1. Pedigrees of sporadic and familial cases examined in this study. Probands are indicated by arrows, asterisk indicates with DNA available.

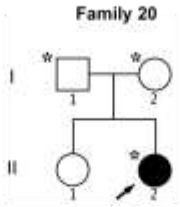


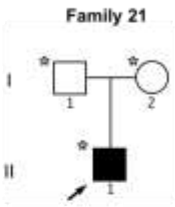

Family 16
I
II
III

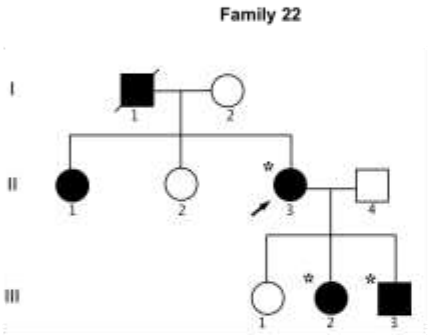

Family 17
I
II

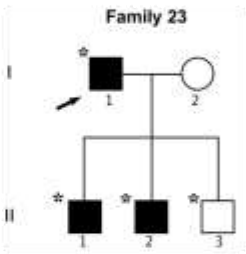

Family 18
I
II

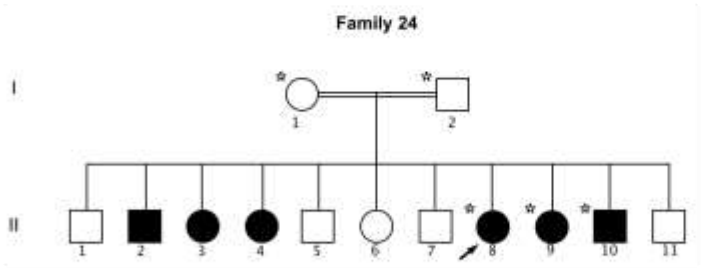

Family 19
I
II

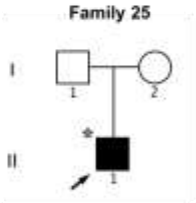

Family 20
I
II

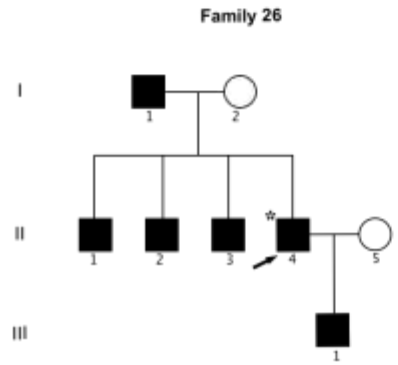

Family 21
I
II

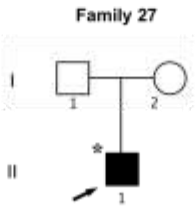

Family 22
I
II
III

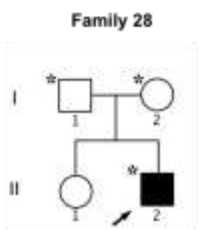

Family 23
I
II

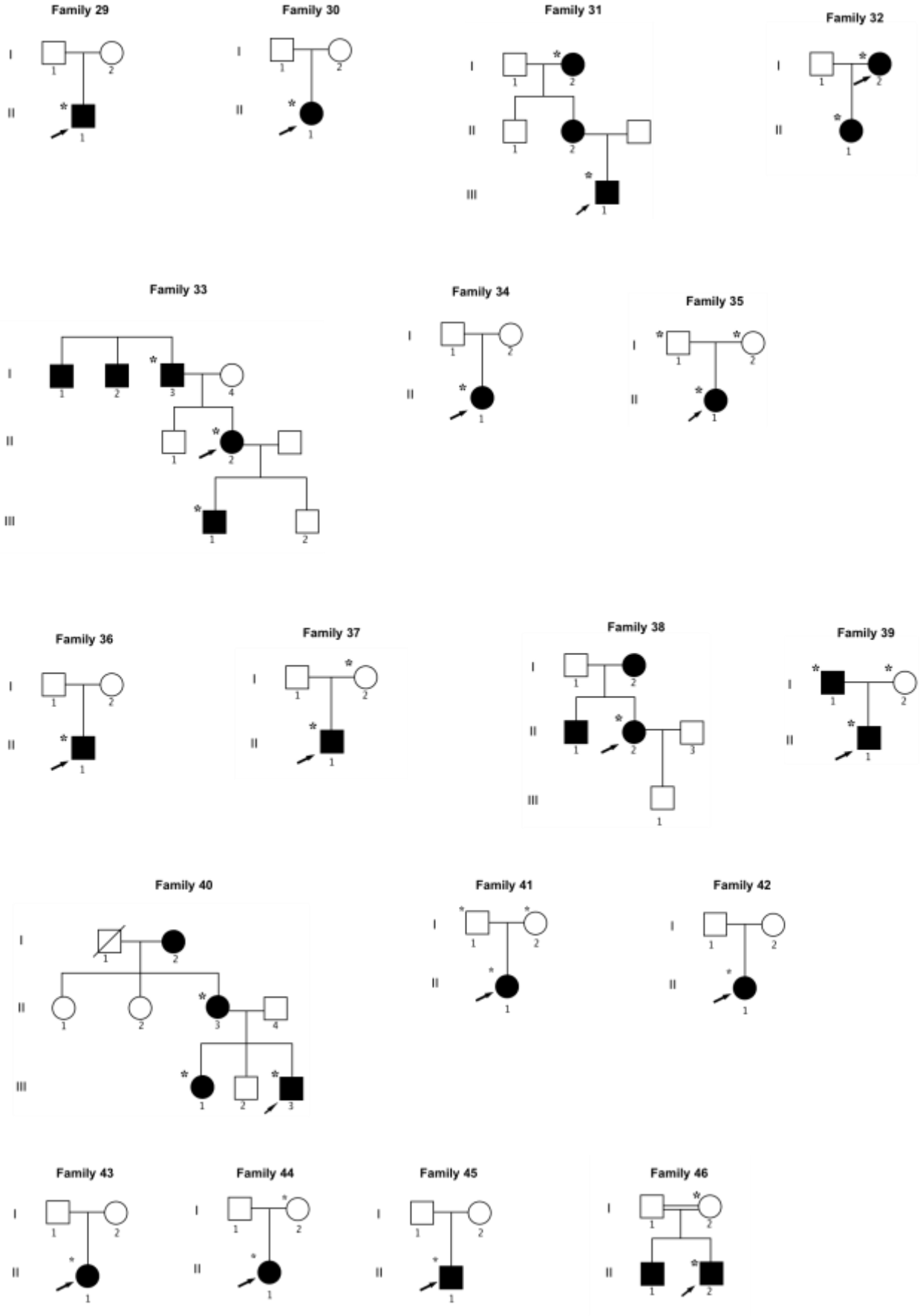

Family 24
I
II


Family 25
I
II

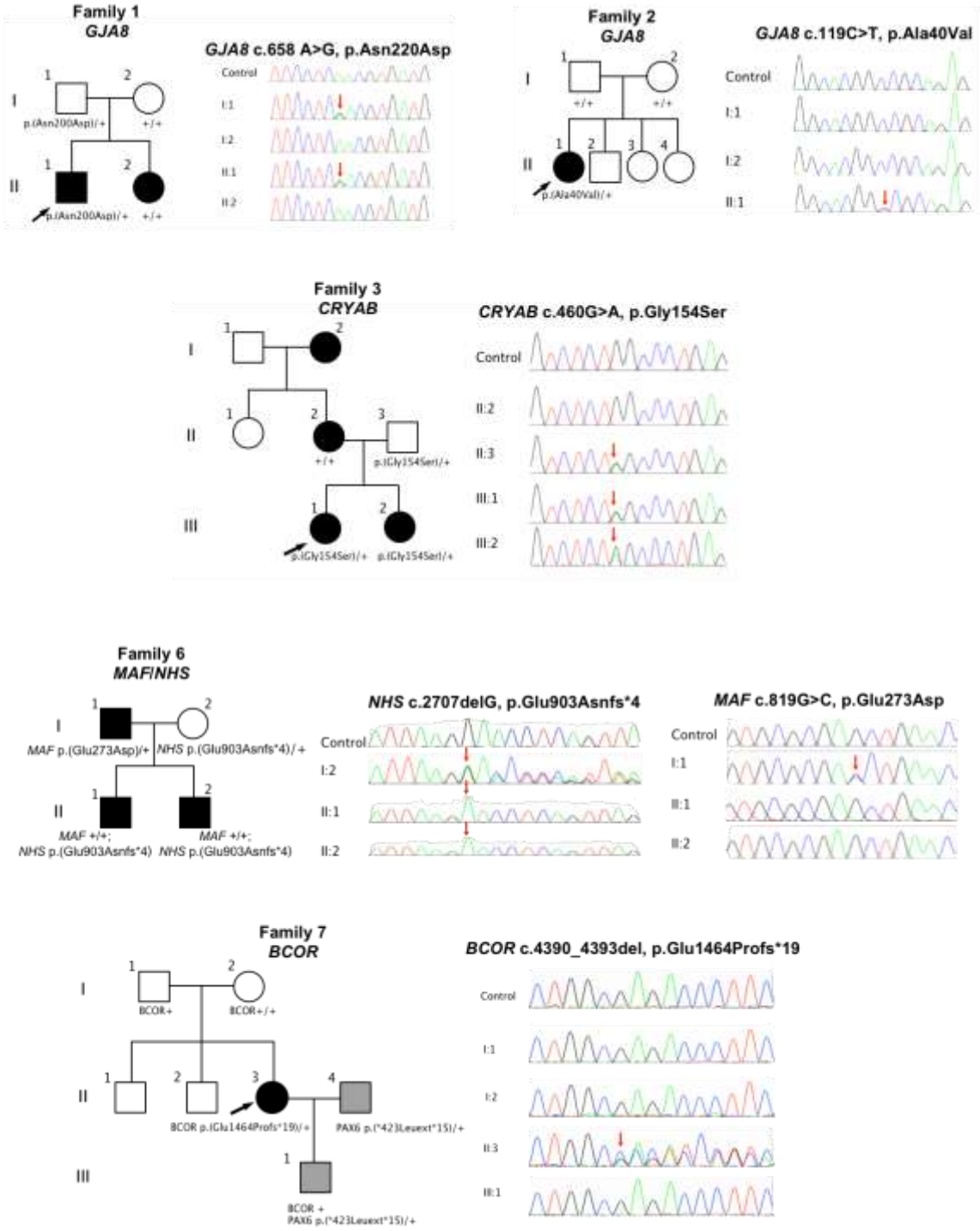

Family 26
I
II
III


Family 27
I
II

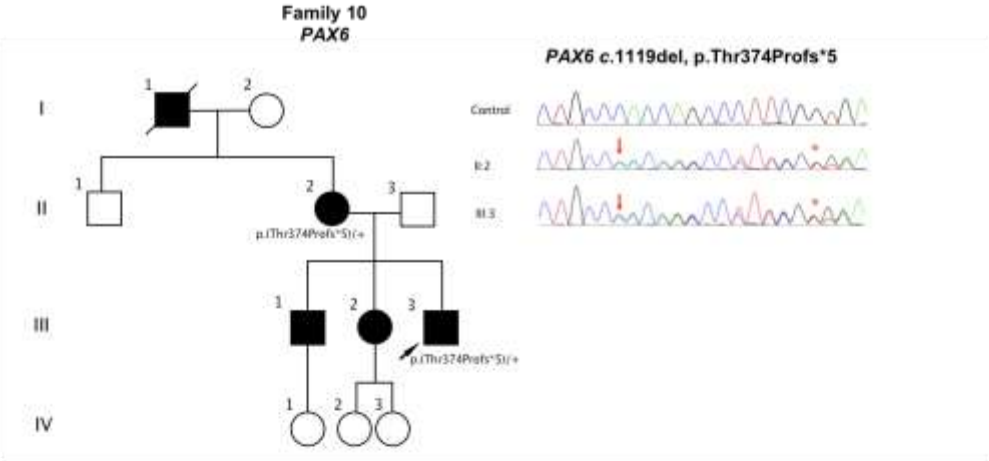

Family 28
I
II

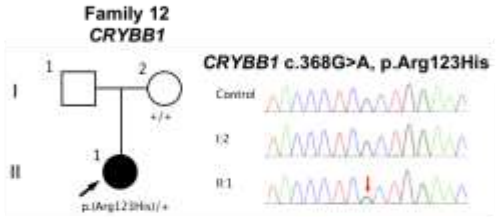

Family 29
Family 30
Family 31
Family 32
Family 33
Family 34
Family 35
Family 36
Family 37
Family 38
Family 39
Family 40
Family 41
Family 42
Family 43
Family 44
Family 45
Family 46

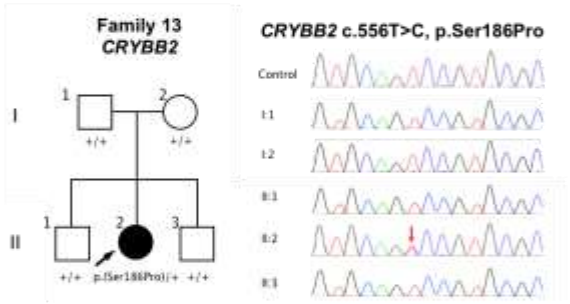
Supp. Figure S2. Pedigrees with variants and Sanger sequencing results.

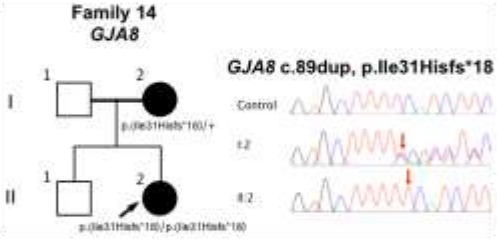


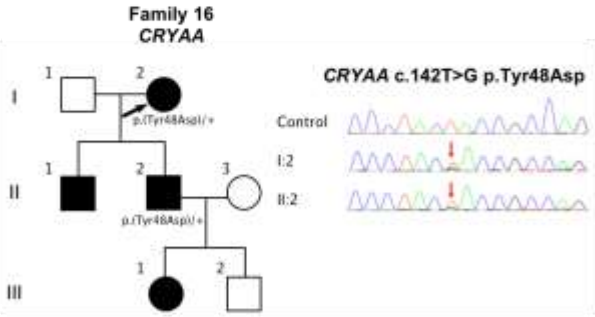
Note: Family 7 is previously reported in the literature (Willcock, et al., 2006) with a *PAX6* c.1268A>T, p.(*423Leuext*15) mutation in the father (II:4) and son (III:1) with variant aniridia (highlighted in grey in the pedigree). Family 8 was previously reported in the literature (Prokudin, et al., 2014).

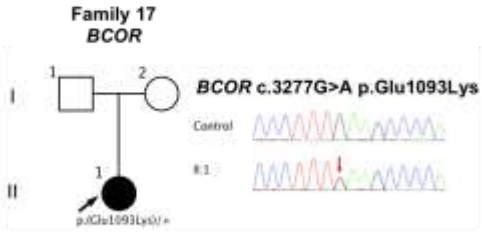

Family 10
PAX6
PAX6 c.1119del, p.Thr374Profs*5
I
II
III
IV
Control
II:2
III:3
p.(Thr374Profs*5)(+
p.(Thr374Profs*5)(+

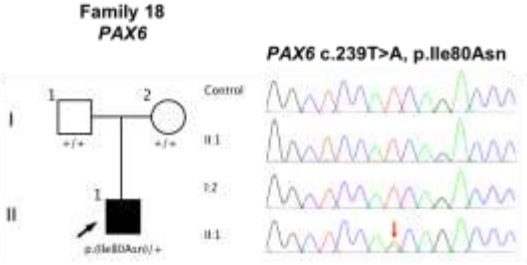

Family 12
CRYBB1
CRYBB1 c.368G>A, p.Arg123His
I
II
Control
I:2
II:1
+/+
p.(Arg123His)(+

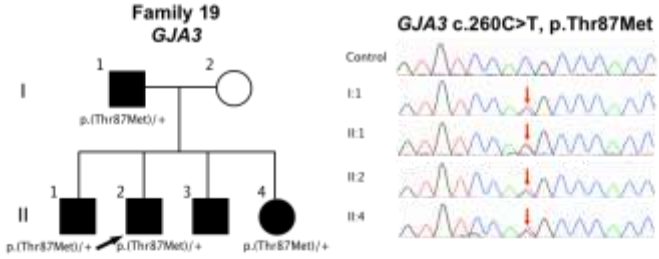

Family 13
CRYBB2
CRYBB2 c.556T>C, p.Ser186Pro
I
II
Control
I:1
I:2
II:1
II:2
II:3
+/+
+/+
+/+
p.(Ser186Pro)(+
+/+

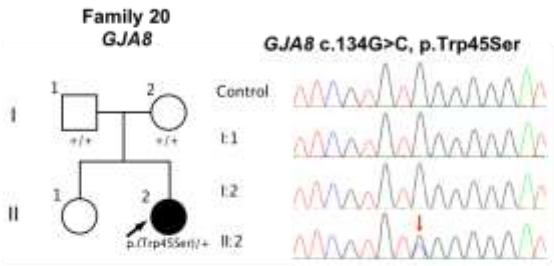

Family 14
GJA8
GJA8 c.89dup, p.Ile31Hisfs*18
I
II
Control
I:2
II:2
p.(Ile31Hisfs*18)(+
p.(Ile31Hisfs*18)(p.(Ile31Hisfs*18)

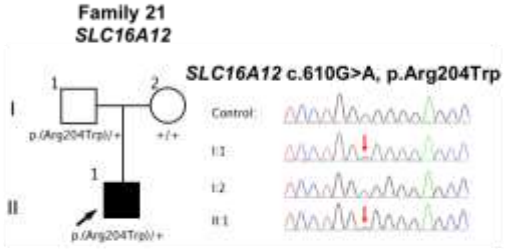

Family 16
CRYAA
CRYAA c.142T>G p.Tyr48Asp
I
II
III
Control
I:2
II:2
p.(Tyr48Asp)(+
p.(Tyr48Asp)(+

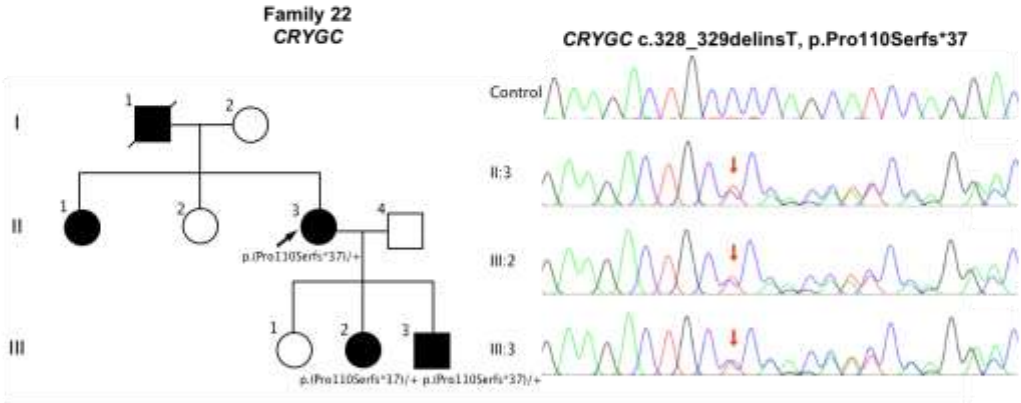

Family 17
BCOR
BCOR c.3277G>A p.Glu1093Lys
I
II
Control
II:1
p.(Glu1093Lys)(+

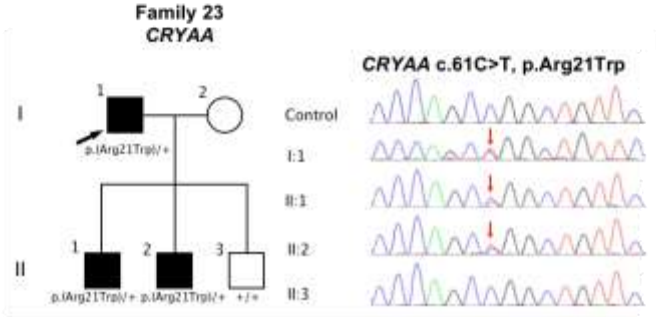

Family 18
PAX6
PAX6 c.239T>A, p.Ile80Asn
I
II
Control
II:1
I:2
II:1
+/+
+/+
p.(Ile80Asn)(+

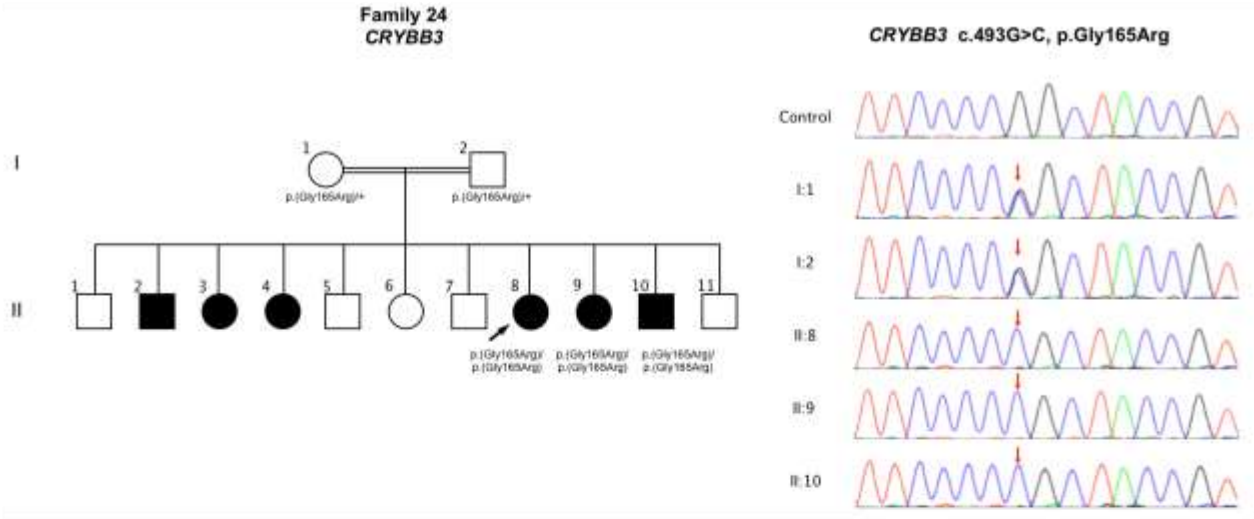

Family 19
GJA3
GJA3 c.260C>T, p.Thr87Met
Control
I:1
II:1
II:2
II:4
p.(Thr87Met)/+

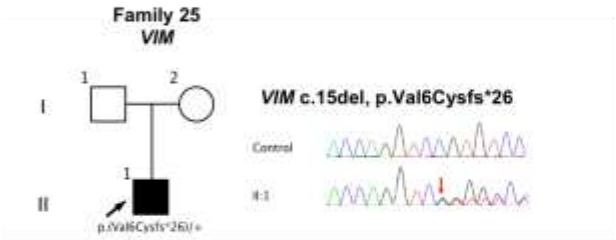

Family 20
GJA8
GJA8 c.134G>C, p.Trp45Ser
Control
I:1
I:2
II:2
p.(Trp45Ser)/+

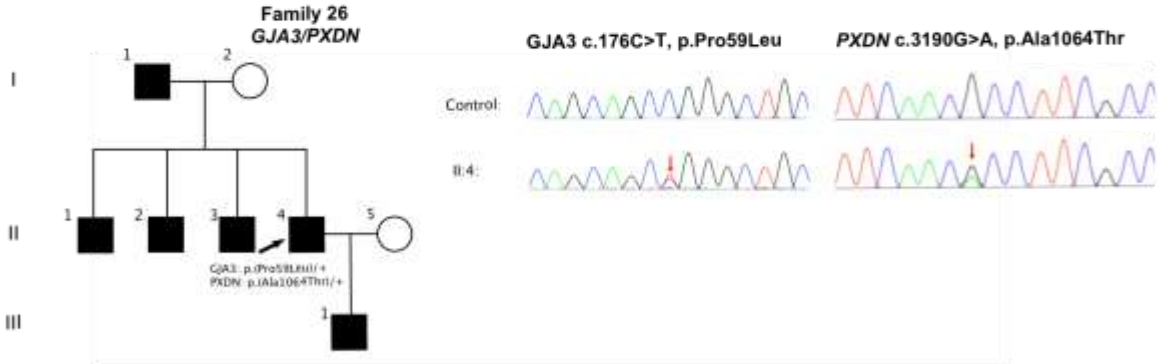

Family 21
SLC16A12
SLC16A12 c.610G>A, p.Arg204Trp
Control
I:1
I:2
II:1
p.(Arg204Trp)/+

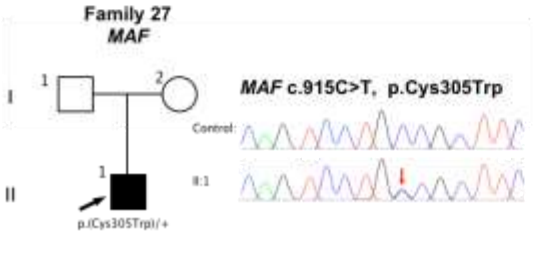

Family 22
CRYGC
CRYGC c.328_329delinsT, p.Pro110Serfs*37
Control
II:3
III:2
III:3
p.(Pro110Serfs*37)/+

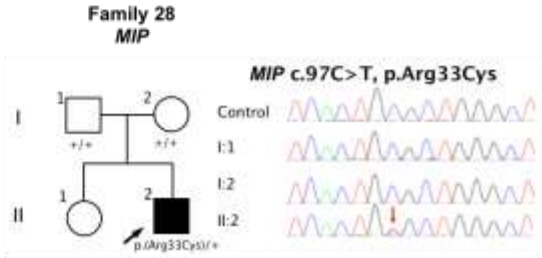

Family 23
CRYAA
CRYAA c.61C>T, p.Arg21Trp
Control
I:1
II:1
II:2
II:3
p.(Arg21Trp)/+

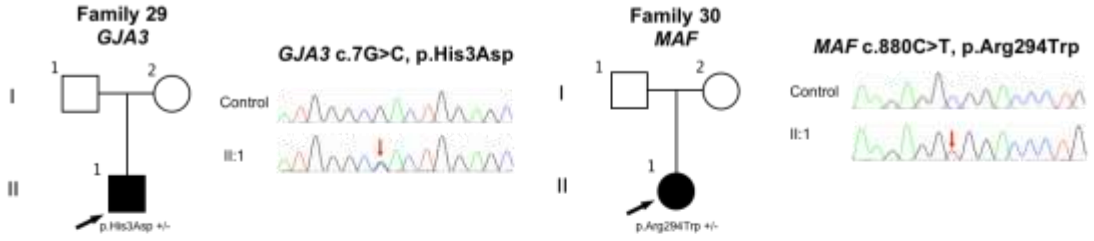

Family 24
CRYBB3
CRYBB3 c.493G>C, p.Gly165Arg
Control
I:1
I:2
II:8
II:9
II:10

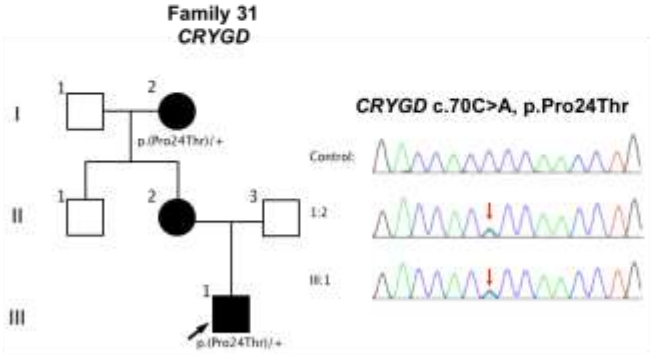

Family 25
VIM
VIM c.15del, p.Val6Cysfs*26
Control
II:1

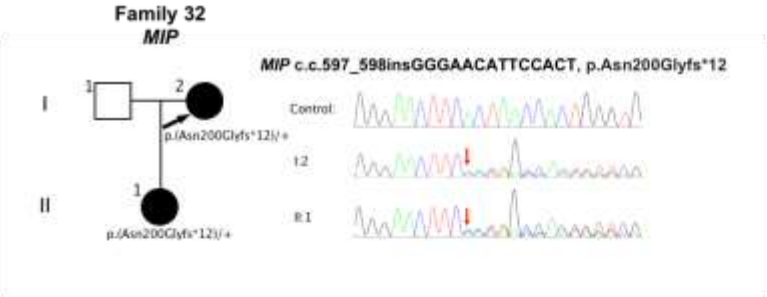

Family 26
GJA3/PXDN
GJA3 c.176C>T, p.Pro59Leu
PXDN c.3190G>A, p.Ala1064Thr
Control
II:4

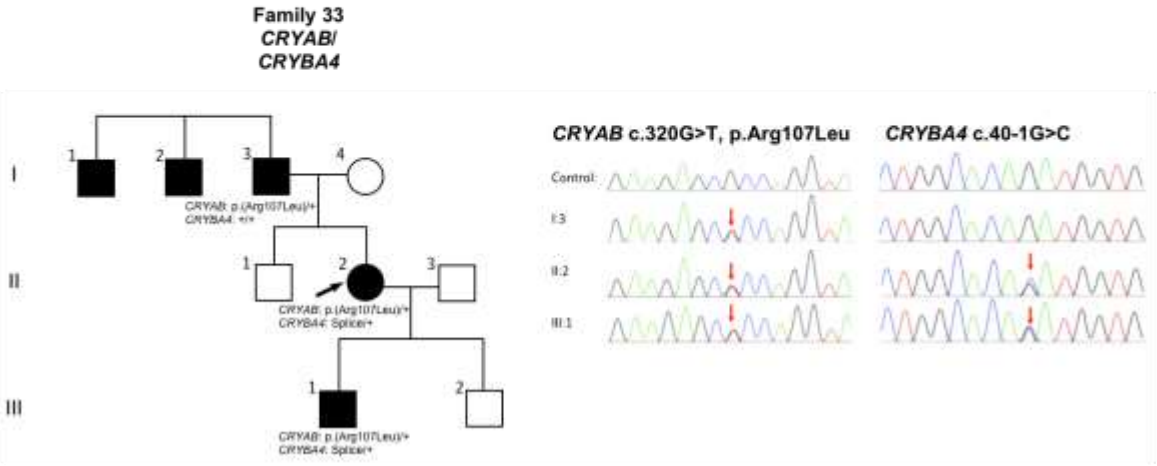

Family 27
MAF
MAF c.915C>T, p.Cys305Trp
Control
II:1

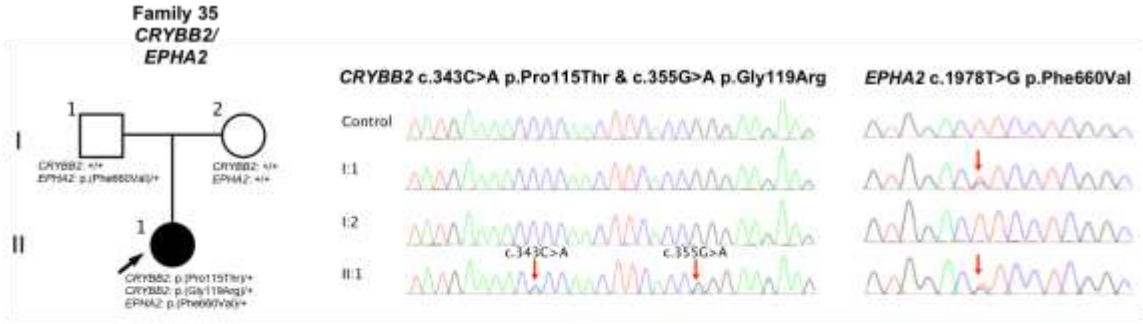

Family 28
MIP
MIP c.97C>T, p.Arg33Cys
Control
I:1
I:2
II:2

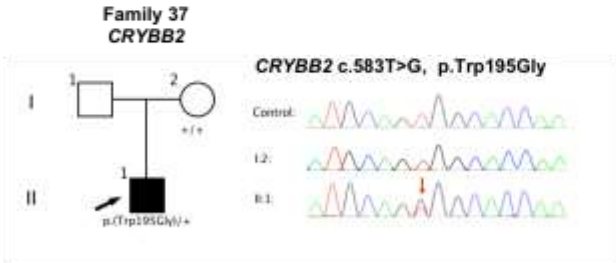

Family 29
GJA3
GJA3 c.7G>C, p.His3Asp
Control
II:1
p.His3Asp +/-
Family 30
MAF
MAF c.880C>T, p.Arg294Trp
Control
II:1
p.Arg294Trp +/-

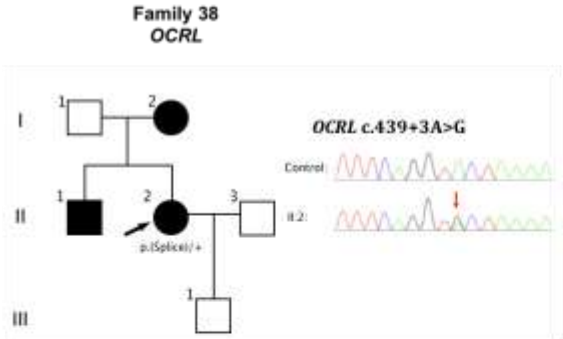

Family 31
CRYGD
CRYGD c.70C>A, p.Pro24Thr
p.(Pro24Thr)/+
Control
II:2
III:1
p.(Pro24Thr)/+

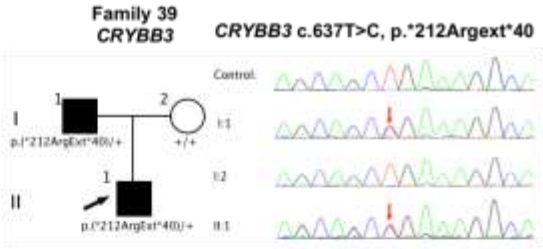

Family 32
MIP
MIP c.c.597_598insGGGAACATTCCACT, p.Asn200Glyfs*12
p.(Asn200Glyfs*12)/+
Control
II:2
II:1
p.(Asn200Glyfs*12)/+

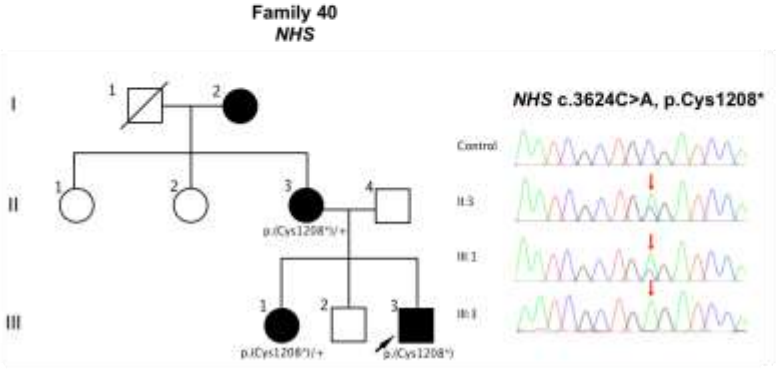

Family 33
CRYAB/
CRYBA4
CRYAB c.320G>T, p.Arg107Leu
CRYBA4 c.40-1G>C
Control
II:3
II:2
III:1

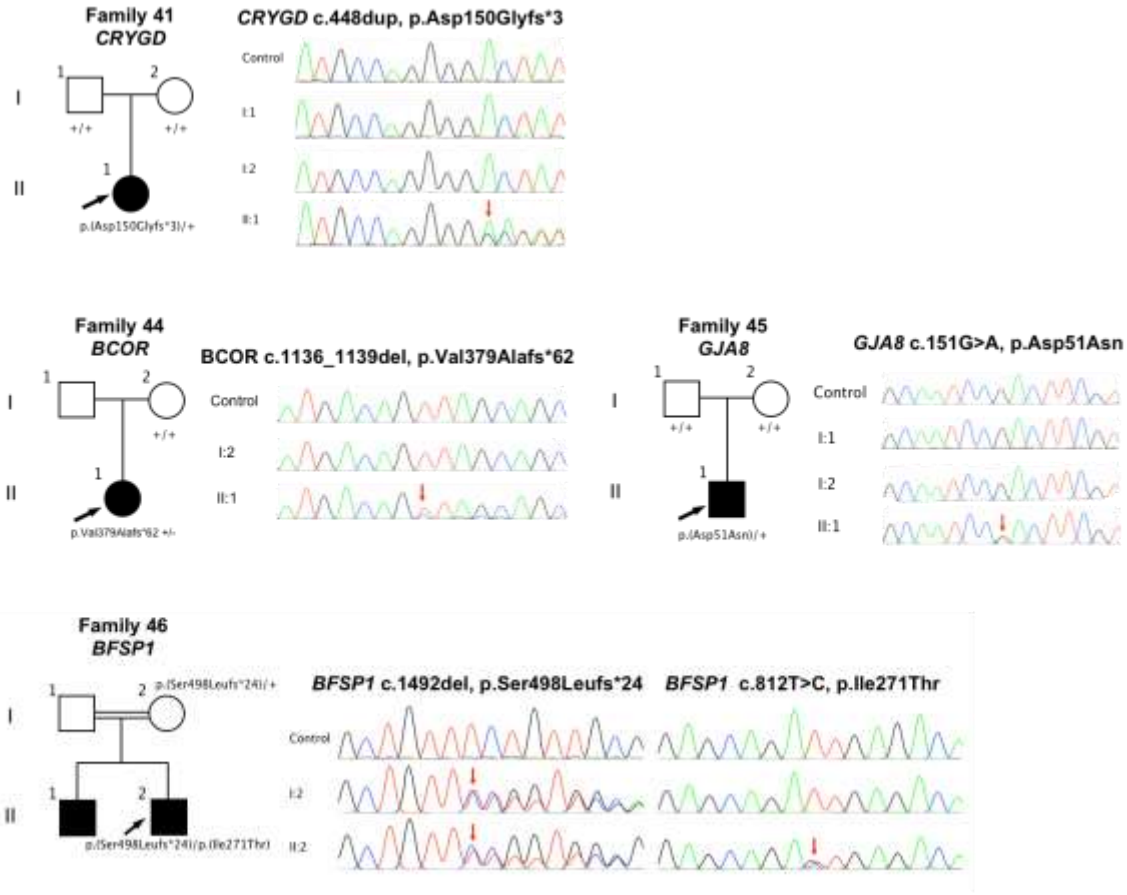

Family 35
CRYBB2/
EPHA2
CRYBB2 c.343C>A p.Pro115Thr & c.355G>A p.Gly119Arg
EPHA2 c.1978T>G p.Phe660Val
Control
I:1
I:2
II:1
c.343C>A
c.355G>A


Family 37
CRYBB2
CRYBB2 c.583T>G, p.Trp195Gly
Control
I:2
II:1


Family 38
OCRL
OCRL c.439+3A>G
Control
II:2


Family 39
CRYBB3
CRYBB3 c.637T>C, p.*212Argext*40
Control
I:1
I:2
II:1


Family 40
NHS
NHS c.3624C>A, p.Cys1208*
Control
II:3
III:1
III:3


Family 41
CRYGD
CRYGD c.448dup, p.Asp150Glyfs*3
Control
I:1
I:2
II:1
Family 44
BCOR
BCOR c.1136_1139del, p.Val379Alafs*62
Family 45
GJA8
GJA8 c.151G>A, p.Asp51Asn
Family 46
BFSP1
BFSP1 c.1492del, p.Ser498Leufs*24
BFSP1 c.812T>C, p.Ile271Thr

Supp. Table S1. Clinical features in 46 families with sporadic and familial cataracts

Family (Proband)	Cataract description	Procedures, age	HCD	AXL	Additional features	Family Information
1 (II:1) F	BL	Baerveldt tube 30yo, cyclodiode photoablation 20yo	L10 R10 35yo	L 28.2, R 27.28 35yo	Aphakic glaucoma Retinal detachment 30yo	Sister less severely affected BL cataracts. Mother sutural cataract. Father unaffected.
2 (II:1) S	BL dense with anterior polar component	Lensectomy 2 weeks, left Baerveldt tube 18mo inserted	L9 R9 birth	L18.4 R 18.55 birth	Aphakic glaucoma, nystagmus VA R 6/30 L 6/60	Parents unaffected
3 (III:1) F	BL rudimentary lens on ultrasound	Lensectomies 5yo	L9.5 R9 9yo	L 24.8 R 25.6 9yo	BL sclerocornea, nystagmus VA 2/60	Sister BL cataracts, Mother BL cataracts, Father unaffected
4 (II:5) F	BL	Bilateral needlings Age 5	L10 R10	L 27.21 R 27.66 Age 65	microcornea	4 affected of 5 siblings. Father and nephew also affected
5 (I:2) F	BL nuclear	Lensectomy 2yo	L11 R11 38yo	N/K	VA L2/60 R3/60	2 daughters have congenital nuclear cataracts/microphthalmia and microcornea HCD 10.5mm
6 (II:1) F	BL dense central nuclear	BL lensectomy 3mo, YAG capsulotomy 7mo BL Baerveldt tube 2.5yo	10mm BL 1yo	17mm BL 1yo	Intellectual disability, large teeth, dysmorphic facies	Brother HCD 11.25 AXL 20.88, aphakic glaucoma, Baerveldt tube 3yo, Father cerulean cataracts HCD 12 AXL 24.5. Mother unaffected
7 (II:3) S	R Microphthalmia and BL cataracts	Bilateral Lensectomies Age 15,Right Molteno implant	L 9 R 11.5	L 23.65 R 19.58 Age 47	nil	Parents unaffected
8 (I:2) F	BL nuclear	BL lensectomy 2yo, L eye glaucoma and enucleation	N/K	N/K	nil	BL cataracts in affected children
9 (II:1) S	BL microphthalmia and total cataracts	R lensectomy age 11	7.5 BL, 12yo	L23, R24 12yo	nil	Parents unaffected, Consanguineous family
10 (III:3) F	Right small central anterior capsular	BL Ptosis surgery	R11.4 L11.9 25yo	22.57R 22.62L 25yo	VA R6/12 L6/12, nystagmus, limbal stem cell failure, OCT shows loss of foveal pit, ectropion uvea	Sister VA R6/24 L6/12, anterior polar cataracts, limbal stem cell failure, OCT shows loss of foveal pit, ectropion uvea, fine rotatory nystagmus, Mother VA R 6/36+1, L NPL, cataracts, glaucoma, limbal stem cell failure, OCT shows loss of foveal pit, ectropion uvea, AXL R21.96 HCD R12.7
11 (II:1) F	BL nuclear	Lensectomy R, 1 month; & L, 4 years	L9.5, R10, 1mth	L17.49 R17.02 1mth	nil	Father also affected
12 (II:1) S	BL posterior subcapsular	BL lensectomy 4yo, IOL implants 9yo	L10 R10 4yo	L17.8, R17. 9 4yo	VA R6/12, L6/19, 12yo	Both parents unaffected
13 (II:1) S	BL	BL lensectomy 3mo, intraocular lens 11yo	N/K	N/K	NK	Both parents unaffected
14 (II:2) F	BL	BL lensectomy 6 mo, glaucoma filtration and 5FU 18yo, Molteno implant 19yo	9.5 BL 24yo	23.5 BL 24yo	Severe glaucoma, 17yo, VA R6/15 L unobtainable	Unaffected sibling, Mother has nuclear dot cataracts and early L posterior subcapsular cataract, HCD 10.5mm.
15 (II:1) S	BL	N/K	9 BL 45yo	L25.2 R 23.7 45yo	VA 6/60 BL 45yo	N/K
16 (I:2) F	BL posterior cortical and diffuse fine dot opacities	radial keratotomy 38yo	N/K	N/K	glaucoma, VA R6/6, L6/15	Granddaughter posterior cortical and fine dot cataracts at 5yo, VA R6/18 L6/36, Son zonular/pulverulent cataracts with central dot opacity at 12yo, VA 6/7.5 7/7
17 (II:1) S	BL	BL IOL 5mo	N/K	N/K	L retinal detachment 7yo	Both parents unaffected
18 (II:1) S	BL anterior polar with nuclear component	Lensectomy/IOL 6mo, L medial rectus resection & L lateral rectus recession for exotropia 8yo	10 BL 6mo	17.2 BL 6mo	nystagmus, VA 6/24 BL	Both parents unaffected
19 (II:2) F	BL lamellar with anterior/posterior sutural component	N/K	N/K	N/K	nil	Father, paternal uncle, grandfather, siblings also affected. Pulverulent in father. Siblings faint/mild cataracts only.

Family (Proband)	Cataract description	Procedures, age	HCD	AXL	Additional features	Family Information
20 (II:2) S	BL anterior cortical/nuclear	BL lensectomy 2 mo	9 BL 3yo	R 15 L 15.2 2 mo	VA 6mo R6/280 L6/120 latent nystagmus	Both parents unaffected
21 (II:1) S	BL lamellar with posterior subcapsular component	BL lensectomy and IOL implant 5yo	N/K	N/K	learning difficulties	Both parents unaffected
22 (II:3) F	BL lamellar	BL cataract surgery age 35	N/K	N/K	nil	Two children affected with lamellar cataracts. Father and sister also affected
23 (I:1) F	BL	BL lensectomy 18mo	N/K	N/K	Glaucoma, severe visual loss	BL cataracts in two sons
24 (II:8) F	BL central dense nuclear with extension to anterior polar	BL Lensectomy	10mm BL	N/K	Nystagmus, microphthalmia, VA 2/60 BL 17yo	6/11 children affected, both parents unaffected.
25 (II:1) S	BL	BL lensectomy 1yo	11.25 BL 1yo	N/K	VA 6/36 BL 1yo	Both parents unaffected
26 (II:4) F	BL lamellar	L lensectomy age 15	N/K	N/K	nil	Father, 3 siblings & son affected
27 (II:1) S	BL	BL lensectomy 6mo R Baerveldt implant 5yo	11.5 BL 5yo	N/K	aphakic glaucoma, corneal ulcers 3yo, VA R6/60 L6/24 5yo	Both Parents unaffected
28 (II:2) S	BL dense central nuclear	lensectomies 1mo	N/K	N/K	N/K	Both parents unaffected
29 (II:1) S	BL nuclear pulverulent	R lens aspiration 17yo L 19yo, R capsulotomy 19yo, IOL R 31yo, L 32yo	N/K	N/K	VA R6/18 L 6/45	Both parents unaffected
30 (II:1) S	BL	Lensectomies 4mo	10.5 BL 4mo	R18 L19 4mo	VA 6/80 BL 2yo	Both parents unaffected
31 (III:1) F	BL Lamellar	BL Lensectomies	10.5L 10R 6mo Age 3 mths	R17.27 L17.38 Age 3 mths	Nil	Mother (II:2) BL cataract and glaucoma, HCD 11BL Grandmother (I:2) also glaucoma and cataracts, HCD 11BL.
32 (I:2) F	BL lamellar & pulverulent with blue dot	BL Phaco + PCIOL Age 65	N/K	R 24.59, L 24.9	Nil	Daughter (II:1) affected more severely requiring cataract surgery Age 31 (R) and 36 (L) yrs
33 (II:2) F	BL lens opacities with 'frosted glass' appearance	nil	N/K	N/K	N/K	Son (III:1) cataracts at 18mo, lensectomies 6yo, father (I:3) and 2 uncles also with cataracts.
34 (II:1) S	BL	N/K	N/K	N/K	N/K	Both parents unaffected
35 (II:1) S	BL	BL lensectomies 2mo	R7 L8 2yo	R 17.23 L 17.93 2yo	VA 6/80 BL 2yo, nystagmus	Both parents unaffected
36 (II:1) S	BL	lensectomy 6yo, YAG capsulotomy 10yo	N/K	N/K	VA R6/24 L6/15 12yo, mild learning difficulties	Both parents unaffected
37 (II:1) S	BL anterior polar	L cataract extract and IOL 11yo, esotropia correction 14yo	N/K	N/K	L amblyopia, VA R6/6 L count fingers 19yo	Both parents unaffected
38 (II:2) F	BL	Cataract needling, childhood	N/K	N/K	Aphakic glaucoma, buphthalmos, scleromalacia,	Mother (I:2) cataracts, brother (II:1) cataracts and nonverbal/intellectual disability, son (III:1) unaffected
39 (II:1) F	BL	BL lensectomies 2mo	10.5 BL 1yo	N/K	Umbilical hernia	Father (I:1) also cataract, glaucoma, umbilical hernia, BL iridectomies with iris cysts. VA R6/18 L6/12 40yo. HCD 11 BL, mother (I:2) unaffected
40 (III:3) F	BL	BL cataract extraction and glaucoma surgery	N/K	N/K	Left foot insertional polydactyly, ADHD, Mild intellectual delay. Face: small narrow teeth with serrated edge, simple ears. VA R unobtainable L6/36	Mother BL subcapsular cataracts diagnosed 32yo, Sister BL cataracts diagnosed 5yo, oligodontia. Grandmother cataracts diagnosed in 50s. Father unaffected.
41 (II:1) S	BL Fetal Nuclear	BL Lens aspirations and PCIOL implants age 8 weeks	N/K	N/K	VA R 6/140, L 6/140	Father tiny dot opacities. Brother and mother unaffected

Family (Proband)	Cataract description	Procedures, age	HCD	AXL	Additional features	Family Information
42 (II:1) S	BL	Bilateral lens aspiration and IOL implants Age 23 months	N/K	L 22.23mm R 22.42	VA R 6/18 L 6/9	Both Parents unaffected
43 (II:1) S	BL anterior polar	N/K	N/K	N/K	N/K	Both parents unaffected
44 (II:1) S	BL	Bilateral Lens aspirations 4 weeks Baerveldt implants	N/K	N/K	VA R6/35, L 6/30 Congenital cleft palate, Atrial septal defect	Both parents unaffected
45 (II:1) S	BL	Right N/K Left No surgery	R 5mm, L unmeas	R 15.82, L unmeas	BL microphthalmia/ sclerocornea	Both parents unaffected
46 (II:2) F	BL	BL cataract extraction 2yo	N/K	N/K	VA R6/19 L6/9.5,glaucoma	Brother also affected. Parents related. Father N/K. Mother unaffected

F Familial, S Sporadic, L left, R right, VA visual acuity, BL bilateral, PC Posterior chamber, IOL Intraocular Lens, Phaco phacoemulsification, HCD Horizontal Corneal Diameter in mm and age of measurement, AXL Axial Length in mm and age of measurement, BL Bilateral, N/K Not known, unmeas Unmeasurable.

Supp. Table S2. List of 32 Cataract Genes

Group	Gene	OMIM number	Inheritance	Chromosome, Gene coordinates (HG19)	Reference Sequence
Crystallins	*CRYAA*	123580	AD or AR	21:44589118-44592915	NM_000394.3
	CRYAB	123590	AD or AR	11:111779289-111794446	NM_001885.2
	CRYBA1	600929	AD	22:26995242-27014052	NM_005208.4
	CRYBA4	123630	AD	22:25595817-25603330	NM_001886.2
	CRYBB1	123610	AD or AR	17:27573881-27581512	NM_001887.3
	CRYBB2	600836	AD	2:219854911-219858143	NM_000496.2
	CRYBB3	123631	AR	22:27017928-27026636	NM_004076.4
	CRYGC	123680	AD	2:208992861-208994554	NM_020989.3
	CRYGD	123690	AD	2:208986331-208989225	NM_006891.3
	CRYGS	123730	AD	3:186256230-186264491	NM_017541.2
Gap Junction	*GJA3*	121015	AD	13:20712394-20735188:	NM_021954.3
	GJA8	600897	AD or AR	1:147374946-147381393	NM_005267.4
Intermediate Filament	*BFSP1*	603307	AR	20:17474550-17549865	NM_001195.4
	BFSP2	603212	AD	3:133118839-133194066	NM_003571.3
	VIM	193060	AD	10:17270258-17279592	NM_003380.3
Lens Membrane	*MIP*	154050	AD	12:56843286-56862950	NM_012064.3
	LIM2	154045	AR	19:51883163-51891214	NM_001161748.1
	SLC16A12	611910	AD	10:91190051-91316398	NM_213606.3
Transcription Factors	*PAX6*	607108	AD	11:31806340-31839509	NM_0001604.4
	MAF	177075	AD	16:79619740-79634611	NM_001031804.2
	HSF4	602438	AD or AR	16:67197288-67203848	NM_001538.3
	FOXE3	601094	AD	1:47881744-47883723	NM_012186.2
	EYA1	601653	AD	8:72109668-72274467	NM_000503.5
	PITX3	602669	AD	10:103989943-104001231	NM_005029.3
Syndromal Genes	*NHS*	300457	X	X:17393543-17754114	NM_198270.3
	OCRL	300535	X	X:128673826-128726538	NM_001587.3
	BCOR	300485	X	X:39909068-40036582	NM_001123385.1
	FTL	134790	AD	19:49468558-49470135	NM_000146.3
	GALK1	604313	AR	17:73747675-73761792	NM_000154.1
Other lens proteins	*GCNT2*	600429	AR	6:10492456-10629601	NM_145655.3
	EPHA2	176946	AD or AR	1:16450832-16482582	NM_004431.3
	PXDN	605158	AR	2:1635659-1748624	NM_012293.2

Supp. Table S3A. TruSeq/MiSeq analysis and variant prioritization

Patient	Aligned Reads	Average Coverage	% over 15X coverage	Unique exonic/splice SNP/indels in 32 cataract genes	synonymous variants	Minor Allele Freq >1%	lacking conservation and predicted pathogenicity	variants of interest
1	1947019	1577	93%	3	2	0	0	1
2	1926038	1566	93%	4	2	1	0	1
3	1791030	1448	93%	2	0	0	1	1
4	1590658	1149	92%	0	0	0	0	0
5	1635604	1334	92%	1	0	1	0	0
6	1642793	1332	93%	5	1	1	2	1
7	1672787	1352	93%	1	1	0	0	0
8	1354442	1114	93%	1	0	0	0	1
9	2029840	1675	93%	0	0	0	0	0
10	2035779	1672	93%	2	0	0	1	1
11	1890361	1539	93%	0	0	0	0	0
12	1793437	1455	93%	1	0	0	0	1
13	1663335	1341	93%	1	0	0	0	1
14	1874139	1517	94%	2	1	0	0	1
15	1670009	1340	93%	0	0	0	0	0
16	669456	461	89%	1	0	0	0	1
17	1563096	1068	91%	1	0	0	0	1
18	802168	549	91%	2	0	1	0	1
19	925550	635	91%	1	0	0	1	0
20	1007310	690	91%	2	1	0	0	1
21	856906	587	90%	3	0	0	2	1
22	667598	457	90%	2	0	0	1	1
23	1004618	689	91%	1	0	0	0	1
24	972188	668	90%	2	0	0	1	1
25	1043798	711	90%	1	0	0	0	1
26	891564	613	91%	1	0	0	0	1
27	941480	649	90%	1	0	0	0	1
28	1048322	719	91%	2	0	1	0	1
29	899930	615	90%	0	0	0	0	0
30	736712	504	90%	0	0	0	0	0
31	973224	667	91%	2	0	0	1	1
32	972896	670	90%	2	0	0	1	1
33	1015392	694	91%	2	0	0	0	2
34	674422	460	88%	1	0	0	1	0
35	795834	546	89%	3	0	0	0	3
36	913398	625	90%	0	0	0	0	0
37	879880	602	91%	2	1	0	0	1
38	646364	444	88%	2	1	0	0	1
AVERAGE	**1247878**	**940**	**91%**					

Supp. Table S3B. TruSight/HiSeq analysis and variant prioritization

Patient	Aligned Reads	Average Coverage	% over 15X coverage	Unique exonic/splice SNP/indels in 32 cataract genes	synonymous variants	Minor Allele Freq >1%	lacking conservation and predicted pathogenicity	variants of interest
1	31502748	182	96%	2	0	0	2	0
3	26431942	164	97%	2	0	0	2	0
4	29134056	176	96%	0	0	0	0	0
5	30545758	208	97%	0	0	0	0	0
7	27837362	189	96%	3	1	1	0	1
9	26920610	182	96%	0	0	0	0	0
11	30663605	174	96%	3	2	1	0	0
15	27067675	153	96%	0	0	0	0	0
17	25494231	166	98%	2	1	0	0	1
19	20113028	113	94%	2	0	0	1	1
21	21039863	143	94%	3	0	2	0	1
26	8859470	59	86%	3	1	0	0	2
29	31191722	174	97%	0	0	0	0	0
30	23699532	157	95%	2	1	0	0	1
34	25213994	172	95%	0	0	0	0	0
36	22807249	126	92%	1	0	1	0	0
38	33088503	222	97%	1	0	0	0	1
39	**10312019**	**106**	**93%**	**1**	**0**	**0**	**0**	**1**
40	**1343330**	**16**	**38%**	**17**	**12**	**2**	**2**	**1**
Father from family 6	**23457813**	**313**	**97%**	**6**	**3**	**1**	**1**	**1**
41	21709480	142	94%	1	0	0	0	1
42	22436003	145	93%	1	0	0	0	1
43	17611667	116	92%	0	0	0	0	0
44	26013957	171	96%	1	0	0	0	1
45	24685912	145	97%	3	2	0	0	1
46	34487134	196	99%	5	2	0	1	2
AVERAGE	**25589370**	**160**	**95%**					

Note: Patients 39, 40 and the father from family 6 (in bold) had TruSight Clinical Exome and are not calculated into averages in final column. All the other patients were sequenced on TruSight One Clinical Exome.

Supp. Table S3C. Gaps on TruSeq

Chromosome	Start	End	Gene
16	79633011	79633948	*MAF*
1	47882391	47882960	*FOXE3*
10	103990597	103991136	*PITX3*
13	20717103	20717481	*GJA3*
X	17393953	17394305	*NHS*
10	103990081	103990420	*PITX3*
1	47881879	47882210	*FOXE3*
20	17511736	17511932	*BFSP1*
1	147380277	147380459	*GJA8*
16	67199753	67199934	*HSF4*
1	47883139	47883317	*FOXE3*
10	103991673	103991851	*PITX3*
10	17271512	17271681	*VIM*
13	20716393	20716558	*GJA3*
X	39923091	39923254	*BCOR*
3	133167379	133167538	*BFSP2*
X	39923617	39923775	*BCOR*
4	111553900	111554057	*PITX2*
22	25599774	25599911	*CRYBB3*
16	67202916	67203053	*HSF4*
20	17489564	17489690	*BFSP1*
22	25601383	25601499	*CRYBB3*
X	39921414	39921527	*BCOR*
2	1664603	1664692	*PXDN*
1	16464197	16464281	*EPHA2*
X	128696310	128696381	*OCRL*
11	31824201	31824269	*PAX6*
2	1747978	1748040	*PXDN*
1	16458100	16458154	*EPHA2*
10	17276500	17276552	*VIM*
X	128674461	128674504	*OCRL*
16	67203272	67203300	*HSF4*
X	128674670	128674677	*OCRL*

Table denotes gaps with <15X coverage on TruSeq, sequenced on Miseq. Arranged by size in descending order.

Supp. Table S3D. Gaps on TruSight

Chromosome	Start	End	Gene
16	79633062	79633367	*MAF*
6	10557377	10557577	*GCNT2*
1	16474871	16474947	*EPHA2*
X	39934379	39934435	*BCOR*
13	20717381	20717429	*GJA3*
1	47882097	47882136	*FOXE3*
1	47881986	47882014	*FOXE3*
2	1677413	1677427	*PXDN*
X	39921997	39922008	*BCOR*
17	73761211	73761219	*GALK1*

Table denotes gaps with <15X coverage on TruSight library, sequenced on HiSeq. Arranged by size in descending order. The gaps in *MAF* and *GJA3* were subsequently covered with Sanger sequencing.

Supp. Table S4. Families with likely non-causative variants

Family (Proband)	Phenotype	Gene (Refseq ID)	Nucleotide change	Predicted Amino acid change	ExAC Minor Allele Frequency	PhyloP, SIFT, MutTaster, PolyPhen	Segregation, other information	Novel	ACMG Classif-ication
Family 1 (II:1)	Congenital cataract, microcornea	*GJA8* NM_005267.4	c.658A>G	p.Asn220Asp	rs138140155 0.00257 (312/121392)	High, D, D, P	No: not present in affected sib, present in unaffected father	(Hansen, et al., 2009)	B
Family 3 (III:1)	Congenital cataract, microcornea, sclerocornea	*CRYAB* NM_001885.2	c.460G>A	p.154Gly>Ser	rs150516929 0.000766 (93/121406)	Mod, T, D, B	No: not present in affected mother, present in unaffected father	(Reilich, et al., 2010)	US
Family 17 (II:1)	Congenital cataract	*BCOR* NM_001123385.1	c.3277G>A	p.Glu1093Lys	rs144736705 0.0002515 (22/87488)	Mod, D, D, P	N/K: parental samples unavailable	No	US
Family 21 (II:1)	Congenital cataract	*SLC16A12* NM_213606.3	c.610C>T	p.Arg204Trp	(1/121240)	Weak, D, D, P	No: present in unaffected father	Yes	US
Family 26 (II:4)	Congenital cataract	*PXDN* NM_012293.2	c.3190G>A	p.Ala1064Thr	rs202132697 0.001965 (230/117030)	High, T, D, P	N/K: parental samples unavailable, mutations in this gene causative when two alleles affected	No	LB
Family 33 (II:2)	Congenital cataract	*CRYBA4* NM_001886.2	c.40-1G>C	intron 2/exon 3 splice site mutation	rs142090709 0.003233 (389/120324)		No: present in affected son, but not affected father	No	B
Family 35 (II:1)	Congenital cataract	*EPHA2* NM_004431.3	c.1978T>G	p.Phe660Val	nil	High, D, D, P	No: present in unaffected father	Yes	US
Family 38 (II:2)	Congenital cataract	*OCRL* NM_001587.3	c.439+3A>G	exon6/intron 6 splice site mutation	rs61752971 0.002418 (212/87693)		N/K: family samples unavailable	No	US

Nucleotide changes are heterozygous unless specified.

D Damaging, P Pathogenic, B Benign, LB Likely Benign, T Tolerated, na not available, N/K not known, US Uncertain Significance. The computational calculations of PhyloP, SIFT, MutationTaster and PolyPhen were performed in Alamut-Visual (Version 2.6, Jan 2015, Interactive Biosoftware, Rouen, France, http://www.interactive-biosoftware.com/alamut-visual/).