Online Resource 2: Summary of WES data for all probands included in this study.

		Whole Exome data				Known cataract (36) and additional crystallin genes (8) data			
Patient #	**Primary Phenotype[a]**	**Target coverage ≥ 10X**	**Mean read depth (target region)**	**Total SNP (exon+ splice) [b]**	**Total indel (exon)**	**Total SNP (exon+ splice)**	**Non-synonymous SNPs**	**Non dbSNP**	**Coding indel**
Patient 1	Congenital cataract; *glaucoma*	85.0%	67X	29,215	1,175	49	13	1	0
Patient 2	Congenital cataract; *microcornea, glaucoma*	84.8%	72X	29,273	1,116	46	11	1	0
Patient 3	Congenital cataract; *glaucoma*	86.1%	91X	30,904	1,330	38	8	1	0
Patient 4	Congenital cataract; *glaucoma, myopia*	82.2%	63X	28,229	1,003	41	14	2	0
Patient 5	Congenital anterior polar cataract	84.1%	67X	28,559	1,039	41	10	0	0
Patient 6	Congenital nuclear cataract, hyperopia, strabismus	83.2%	59X	28,991	1,090	40	6	1	0
Patient 7	Congenital cataract; *glaucoma*	83.4%	62X	28,524	1,053	37	10	2	0
Patient 8	Congenital cataract	81.5%	50X	28,490	982	49	13	0	0
Patient 9	Unilateral or bilateral congenital cataract	83.1%	60X	28,732	1,074	44	11	0	1
Patient 10	Congenital cataract, *strabismus*	88.4%	114X	31,629	1,398	52	12	1	0
Patient 11	Congenital cataract; *pupil defects, glaucoma*	81.6%	53X	27,734	1,000	43	14	1	0
Patient 12	Congenital cataract	85.6%	72X	29,949	1,166	42	9	2	0
Patient 13	Juvenile cataract	83.5%	62X	29,193	1,128	45	9	0	0
Patient 14	Juvenile cataract	83.6%	65X	28,468	1,090	43	11	1	0
Patient 15	Congenital cataract	93.3%	72X	43,433	4,367	79	16	2	0
Patient 16	Congenital cataract	88.1%	71X	43,186	3,950	79	9	0	0
Patient 17	Congenital cataract	96.2%	72X	43,311	4,441	87	13	0	0
Patient 18	Congenital cataract; *microphthalmia/ microcornea, glaucoma, corneal opacity*	95.6%	65X	42,836	4,452	95	14	2	0
Patient 19	Congenital cataract, nystagmus; *glaucoma, corneal opacity*	88.1%	62X	43,489	4,237	88	13	2	0
Patient 20	Juvenile cataract; *glaucoma*	80.6%	72X	39,966	3,635	75	12	0	0
Patient 21	Juvenile cataract (unilateral)	78.6%	59X	43,915	3,816	96	12	1	0
Patient 22	Congenital cataract, microcornea, coloboma, glaucoma, macrocephaly	96.00%	78X	41,164	4,512	92	11	1	0
Patient 23	Early onset adult cataract (40s), retinal detachment	94.9%	68X	43,254	4,401	82	12	2	0

[a]variable features within the family are noted in italics; [b]read depth >=8, score >=20

Online Resource 3: List of known cataract genes evaluated in this study.

Gene	MIM	Locus	Inheritance
FOXE3	601094	1p32	AD
CRYGA	123660	2q33-35	AD
CRYGC	123680	2q33-35	AD
CRYGD	123690	2q33-35	AD
BFSP2	603212	3q21-25	AD
CRYGS	123730	3q27	AD
EYA1	601653	8q13.3	AD
VIM	193060	10p13	AD
SLC16A12	611910	10q23.31	AD
PITX3	602669	10q25	AD
PAX6	607108	11p13	AD
MIP	154050	12q13	AD
GJA3	121015	13q11	AD
MAF	177075	16q22-23	AD
CRYBA1	123610	17q11.1-12	AD
FTL	134790	19q13.3-4	AD
CHMP4B	610897	20q11.21	AD
CRYBA4	123631	22q11.2-13.1	AD
CRYBB2	123620	22q11.2-12.1	AD
EPHA2	176946	1p36	AD or AR
GJA8	600897	1q21.1	AD or AR
SIL1	608005	5q31	AD or AR
CRYAB	123590	11q22.3-23.1	AD or AR
HSF4	602438	16q21-22.1	AD or AR
CRYAA	123580	21q22.3	AR or AD
CRYBB1	600929	22q11.2-12.1	AR or AD
PXDN	605158	2p25.3	AR
GCNT2	600429	6p24	AR
TDRD7	611258	9q22.33	AR
GALK1	604313	17q25.1	AR
LIM2	154045	19q13.4	AR
BFSP1	603307	20p12.1	AR
CRYBB3	123630	22q11.2-12.2	AR
FYCO1	607182	3p21.31	AR
AGK	610345	7q34	AR
NHS	300457	Xp22.13	X

Inh = Inheritance; AD = Autosomal dominant; AR = Autosomal recessive; X = X-linked.

Online Resource 4: Rare and novel variants determined to be non-causative.

Samples with SNP	Gene	Reference sequence	Nucleotide change	Amino acid change	dbSNP	Allele frequency (EVS)	PolyPhen/ SIFT prediction	Cosegregation analysis	Causative mutation
Patient 1	*BFSP1*	NM_001195.3	c.1895C>A	p.(Ser632Tyr)	-	0/8600 EA 0/4352 AA	probably damaging/ deleterious	No cosegregation	-
Patient 1	*CRYGN*	NM_144727.1	c.97C>T	p.(Arg33Trp)	rs145702098	2/8600 EA 0/4406 AA	benign/ deleterious	No cosegregation	-
Patient 2	*GJA8*	NM_005267.4	c.741T>G	p.(Ile247Met)	rs80358202	31/8600 EA 1/4406 AA	benign/ tolerated	No cosegregation	*CRYBB1*
Patient 4	*BFSP2*	NM_003571.2	c.265C>T	p.(Arg89Trp)	-	3/8600 EA 0/4406 AA	probably damaging/ tolerated	No cosegregation	*CRYBA2*
Patient 4	*BFSP2*	NM_003571.2	c.437G>A	p.(Arg146His)	rs148759360	0/8600 EA 0/4406 AA	possibly damaging/ tolerated	No cosegregation	*CRYBA2*
Patient 4	*CRYGS*	NM_017541.2	c.305G>A	p.(Gly102Glu)	rs144124671	5/8600 EA 3/4406 AA	benign/ tolerated	No cosegregation	*CRYBA2*
Patient 7	*GCNT2*	NM_145649.4	c.892G>A	p.(Glu298Lys)	rs139794913	not covered	probably damaging/ tolerated	No cosegregation	*CRYBB3*
Patient 12	*HSF4*	NM_001538.3	c.636G>T	p.(Met212Ile)	-	28/8448 EA 4/4182 AA	possibly damaging/ deleterious	No cosegregation	-
Patient 12	*FYCO1*	NM_024513.3	c.3320A>G	p.(Asn1107Ser)	-	0/8568 EA 0/4390 AA	benign/ tolerated	No cosegregation	-
Patient 18	*SIL1*	NM_022464.4	c.274C>T	p.(Arg92Trp)	rs149242794	1/8600 EA 0/4406 AA	probably damaging/ deleterious	No cosegregation	*CRYGC*
Patient 19	*FYCO1*	NM_024513.3	c.3698G>A	p.(Gly1233Asp)	-	0/8600 EA 0/4406 AA	benign/ tolerated	No cosegregation	-
Patient 19	*AGK*	NM_018238.3	c.952C>T	p.(Arg318Trp)	-	0/8578 EA 0/4392 AA	possibly damaging/ deleterious	No cosegregation	-
Patient 21	*GCNT2*	NM_145649.4	c.35C>T	p.(Ala12Val)	rs150732107	not covered	benign/ tolerated	No cosegregation	-
Patient 23	*FOXE3*	NM_012186.2	c.587G>C	p.(Gly196Ala)	-	not covered	benign/ tolerated	No cosegregation	-
Patient 23	*CRYGD*	NM_006891.3	c.51T>G	p.(Tyr17*)	-	0/8582 EA 0/4384 AA	N/A (truncation)	No cosegregation	-

Whole Exome Sequencing in Dominant Cataract Identifies a New Causative Factor, *CRYBA2*, and a Variety of Novel Alleles in Known Genes.

Human Genetics

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