HONG KONG MEDICAL JOURNAL 香港醫學雜誌

Supplementary material

The supplementary material was provided by the authors and some information may not have been peer reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by the Hong Kong Academy of Medicine and the Hong Kong Medical Association. The Hong Kong Academy of Medicine and the Hong Kong Medical Association disclaim all liability and responsibility arising from any reliance placed on the content.

Supplement to: SSW Cheng, S Cheung, TK Ko, et al. Spectrum of inherited eye disorders at Hong Kong Children's Hospital: insights into the local genetic landscape and experience with ocular genetic services. Hong Kong Med J 2025;Epub 4 Aug 2025. https://doi.org/10.12809/hkmj2412298.

SUPPLEMENTARY TABLE 1. Panel testing (from Genomics England PanelApp)

Panel name	**Version(s) used**
Structural eye disease	v2.0, v3.0 (after March 2023)
Retinal disorders	v2.195, v3.0 (after November 2022), v4.0 (after March 2023)
Stickler syndrome	v3.0, v4.0 (after March 2023)
Anophthalmia or microphthalmia	v1.52
Glaucoma (developmental)	v1.45
Bilateral congenital or childhood-onset cataracts	v2.76, v3.0 (after November 2022), v4.0 (after March 2023)
Corneal dystrophy	v1.2, v2.0 (after November 2022), v3.2 (after March 2023)
Corneal abnormalities	v1.13
Optic neuropathy	v2.2, v3.0 (after November 2022), v4.0 (after March 2023)
Rare multisystem ciliopathy Super Panel	v4.21, v8.2 (after November 2022), v12.2 (after March 2023)
Ocular and oculocutaneous albinism	v1.23
Albinism or congenital nystagmus	v1.2, v2.0 (after November 2022), v3.0 (after March 2023)
Monogenic hearing loss	v2.5, v3.0 (after November 2022), v4.0 (after March 2023)

© 2025 Hong Kong Academy of Medicine Press | CC BY-NC-ND 4.0

SUPPLEMENTARY TABLE 2. Clinical phenotype and genetic diagnosis of patients with positive genetic test results

Patient ID*	Presenting clinical phenotype	Disease category†	Gene (incidental finding)	Variant(s)	Zygosity	Inheritance	Molecular diagnosis
1	Syndromic microcephaly, global developmental delay, thin upper lip, bilateral low-set ears, single palmar crease, pectus excavatum, left high myopia, amblyopia, exotropia, left persistent vasculature, and chromosomal abnormalities	G	*KMT2C*	arr[GRCh37]7q36.1 (149582906_152096737)X1 -2.5 Mb terminal deletion (37 OMIM genes including *KCNH2* and *KMT2C*)	Heterozygous	De novo	Kleefstra syndrome 2 (OMIM#617768)
2	Bilateral retinoblastoma	H	*RB1*	NM_000321.2 (*RB1*): c.1613_1614delCA p.(Ala538Glyfs*16)	Heterozygous	De novo	Retinoblastoma (OMIM#180200)
3	Bilateral anterior chamber features and posterior vitreous opacity Norrie disease	A	*NDP*	NM_000266.4 (*NDP*): c.199G>T p.(Gly67Trp)	Hemizygous	Maternal	Norrie disease (OMIM#310600)

© 2025 Hong Kong Academy of Medicine Press | CC BY-NC-ND 4.0

6	Syndromic brachycephaly, bilateral hearing loss, hypotonia, global developmental delay, bilateral microphthalmia, and retinal dysgenesis	B, D	*SOX2*	NM_003106.4 (*SOX2*): c.758dup p.(Val254Cysfs*56)	Heterozygous	De novo	Microphthalmia, syndromic 3 (OMIM#206900)
8	Bilateral glaucoma, cataract, and retinitis pigmentosa, with a history of diabetes and hypertension	B, C	*EYS*	NM_001142800.2 (*EYS*) exon 15 deletion NM_001142800.2 (*EYS*): c.8309T>C p.(Leu2770Pro)	Compound heterozygous	Incomplete	Retinitis pigmentosa 25 (OMIM#602772)
15	Bilateral retinal detachment, flat facial profile, micrognathia, and joint laxity Stickler syndrome	B	*COL2A1*	NM_001844.2 (*COL2A1*): c.70C>T p.(Gln24Ter) dn	Heterozygous	De novo	Stickler syndrome, type I (OMIM#108300)
16	Bilateral macular dystrophy, poor cone response	B	*PDE6C*	NM_006204.4 (*PDE6C*): c.1784T>G, p.(Met595Arg) NM_006204.4 (*PDE6C*): c.2156T>C, p.(Met719Thr)	Compound heterozygous	In trans	Cone dystrophy 4 (OMIM#613093)
21	Nystagmus, progressive myopia, and reduced cone response Aland Island eye disease	B	*CACNA1F*	NM_005183.4 (*CACNA1F*): c.208_217del p.(Arg70Serfs*28)	Hemizygous	Maternal	Aland Island eye disease (OMIM#300600)

© 2025 Hong Kong Academy of Medicine Press | CC BY-NC-ND 4.0

25	Syndromic mild facial hypoplasia, prominent eyes, hearing loss, retinal degeneration	B	*COL11A1*	NM_001854.4 (*COL11A1*): c.3655-2A>G p.?	Heterozygous	De novo	Marshall syndrome (OMIM#154780)
26	Early onset profound hearing loss and retinitis pigmentosa Usher syndrome	B	*USH2A*	NM_206933.4 (*USH2A*): c.8740C>T p.(Arg2914*) NM_206933.4 (*USH2A*): c.5572+1G>A p.?	Compound heterozygous	Incomplete (father deceased)	Usher syndrome, type 2A (OMIM#276901)
28	Retinoschisis	B	*RS1*	NM_000330.4 (*RS1*): c.452A>C p.(Tyr151Ser)	Hemizygous	Maternal	Retinoschisis (OMIM#312700)
29	Retinoschisis	B	*RS1*	NM_000330.4 (*RS1*): c.214G>A p.(Glu72Lys)	Hemizygous	Maternal	Retinoschisis (OMIM#312700)
30	Familial exudative vitreoretinopathy	B	*LRP5*	NM_002335.4 (*LRP5*): c.3004C>T p.(Arg1002*)	Heterozygous	De novo	Exudative vitreoretinopathy 4 (OMIM#601813)

© 2025 Hong Kong Academy of Medicine Press | CC BY-NC-ND 4.0

33	Bilateral retinitis pigmentosa, nystagmus, cataract, and hand tremor	B,C,E	*PANK2*	NM_153638.4 (*PANK2*): c.655G>A p.(Gly219Ser)	Homozygous	Incomplete (father deceased, mother is heterozygous carrier)	Neurodegeneration with brain iron accumulation 1 (OMIM#234200)
34	Bilateral anterior segment dysgenesis, cataract, developmental delay, and cleft palate	A,C	*PAX6*	NM_000280.4 (*PAX6*): c.718C>T p.(Arg240*)	Heterozygous	De novo	Microphthalmia/coloboma 12 (OMIM#120200)
35	Right retinoblastoma	H	*RB1*	NM_000321.3 (*RB1*): c.1960+1G>A p.?	VAF: 18%	De novo	Retinoblastoma (OMIM#180200)
39	Bilateral retinoblastoma	H	*RB1*	NM_000321.2 (*RB1*): c.1275delC p.(Phe426Leufs*31)	Heterozygous	De novo	Retinoblastoma (OMIM#180200)
40	Optic glioma with café-au-lait spots and neurofibromatosis	H	*NF1*	Heterozygous NM_000267.3 (*NF1*): c.699del p.(Lys233Asnfs*48)	Heterozygous	De novo	Neurofibromatosis, type 1 (OMIM#162200)

© 2025 Hong Kong Academy of Medicine Press | CC BY-NC-ND 4.0

42	Bilateral coronal craniosynostosis, failure to thrive, moderate to severe intellectual disability, microphthalmia, and high myopia	D, G	*CTNNB1*	NM_001098209.1 (*CTNNB1*): c.1759C>T p.(Arg587*)	Heterozygous	De novo	Neurodevelopmental disorder with spastic diplegia and visual defects (OMIM#615075)
44	Bilateral retinitis pigmentosa/choroideraemia	B	*CHM*	NM_000390.4 (*CHM*): c.308dup p.(Tyr103*)	Hemizygous	NA	Choroideremia (OMIM#303100)
46	Syndromic microcephaly, frontal narrowing, hypotelorism, and high myopia	G	*CTNNB1*	NM_001904.4 (*CTNNB1*): c.998dup p.(Tyr333*)	Heterozygous	De novo	Neurodevelopmental disorder with spastic diplegia and visual defects (OMIM#615075)
48	Syndromic moderate developmental delay, hypotonia, thin lips, hypoplastic alae nasi, high myopia, and divergent squint/exotropia	G	*CTNNB1*	NM_001098209.1 (*CTNNB1*): c.242-1G>C, p.?	Heterozygous	De novo	Neurodevelopmental disorder with spastic diplegia and visual defects (OMIM#615075)

© 2025 Hong Kong Academy of Medicine Press | CC BY-NC-ND 4.0

53	Syndromic presentation with retinal and iris coloboma, facial nerve palsy, Dandy-Walker variant, kyphoscoliosis, hypogonadotropic hypogonadism, and deafness	D	*CHD7*	NM_017780.3 (*CHD7*): c.359delG p.(Gly120Alafs*91)	Heterozygous	De novo	CHARGE syndrome (OMIM#214800)
54	Bilateral coloboma and developmental delay	D	*CHD7*	NM_017780.3 (*CHD7*): c.4480C>T p.(Arg1494*)	Heterozygous	De novo	CHARGE syndrome (OMIM#214800)
56	Bilateral posterior subcapsular cataract and end-stage renal failure Ciliopathy	C	*NPHP1*	Heterozygous deletion of entire *NPHP1* gene; Heterozygous NM_001128178.3 (*NPHP1*): c.1130del p.(Lys377Serfs*55)	Compound heterozygous	In trans	Joubert syndrome 4 (OMIM#609583)
58	Bilateral congenital cataract	C	*GCNT2*	NM_001491.3(*GCNT2*): c.1019A>G p.(Tyr340Cys) NM_001491.3 (*GCNT2*): c.1058del p.(Lys353Serfs*26)	Compound heterozygous	In trans	Cataract 13 with adult i phenotype (OMIM#116700)

© 2025 Hong Kong Academy of Medicine Press | CC BY-NC-ND 4.0

59	Bilateral congenital cataract with nail dystrophy	C	*SREBF1*	NM_004176.4 (*SREBF1*): c.1287dup p.(Ser430Leufs*27)	Heterozygous	Maternal	Ichthyosis, follicular, with atrichia and photophobia syndrome 2 (OMIM#619016)
60	Diabetes, hearing loss, cardiomyopathy, and optic neuropathy	E	*WFS1*	NM_006005.3 (*WFS1*): c.2020G>A p.(Gly674Arg); NM_006005.3 (*WFS1*): c.2170C>T p.(Pro724Ser)	Compound heterozygous	In trans	Wolfram syndrome 1 (OMIM#222300)
64	Syndromic retinitis pigmentosa, bilateral toe polydactyly, impaired glucose tolerance, moderate intellectual disability, and epilepsy Bardet-Biedl syndrome	B	*BBS7*	NM_176824.3 (*BBS7*): c.1002del p.(Asn335Ilefs*47)	Homozygous	In trans	Bardet-Biedl syndrome 7 (OMIM#615984)

© 2025 Hong Kong Academy of Medicine Press | CC BY-NC-ND 4.0

66	Bilateral retinal dystrophy, renal failure, and ciliopathy	B, C	*NPHP1*	arr[GRCh37] 2q13(110859672_110982530)x0 123Kb, homozygous deletion (including *NPHP1*)	Homozygous	In trans (mother tested)	Joubert syndrome 4 (OMIM#609583)
68	Profound hearing loss since age 50 and retinitis pigmentosa Usher syndrome	B	*USH2A*	NM_206933.4 (*USH2A*): c.538T>C p.(Ser180Pro)	Homozygous	In trans	Usher syndrome, type 2A (OMIM#276901)
69	Pierre Robin sequence, cleft palate, flat facial profile, hearing loss Stickler syndrome	B	*COL11A1*	NM_001854.4 (*COL11A1*): c.3655-2A>T p.?	Heterozygous	Maternal	Stickler syndrome, type II (OMIM#604841)
72	Retinoschisis	B	*RS1*	NM_000330.4 (*RS1*): c.329G>A p.(Cys110Tyr)	Hemizygous	Maternal	Retinoschisis (OMIM#312700)
73	Retinoschisis	B	*RS1*	NM_000330.4 (*RS1*): c.214G>A p.(Glu72Lys)	Hemizygous	Maternal	Retinoschisis (OMIM#312700)
76	Bilateral congenital cataract	C	*CRYBA1*	NM_005208.5 (*CRYBA1*): c.215+1G>T p.?	Heterozygous	NA	Cataract 10, multiple types (OMIM#600881)

© 2025 Hong Kong Academy of Medicine Press | CC BY-NC-ND 4.0

77	Macular dystrophy	B	*ABCA4*	NM_000350.3 (*ABCA4*): c.1804C>T p.(Arg602Trp)	Homozygous	In trans	Stargardt disease 1 (OMIM#248220)
78	Bilateral retinitis pigmentosa with history of acute myeloid leukaemia	B	*CRB1*	NM_201253.3 (*CRB1*): c.3676G>T p.(Gly1226*)	Homozygous	In trans	Leber congenital amaurosis 8 (OMIM#613835)
80	Bilateral retinal dystrophy Stargardt disease	B	*ABCA4*	NM_000350.3 (*ABCA4*): c.6563T>C p.(Phe2188Ser) NM_000350.3 (*ABCA4*): c.6284A>T p.(Asp2095Val)	Compound heterozygous	In trans (father deceased)	Stargardt disease 1 (OMIM#248220)
82	Autosomal dominant optic atrophy, slowly progressive	E	*OPA1*	NM_130837.2 (*OPA1*): c.190_194del p.(Ser64Aspfs*7)	Heterozygous	NA	Optic atrophy 1 (OMIM#165500)
85	Bilateral occult macular dystrophy	B	*RP1L1*	NM_178857.6 (*RP1L1*): c.133C>T p.(Arg45Trp)	Heterozygous	NA	Occult macular dystrophy (OMIM#613587)
87	Bilateral optic atrophy/hereditary optic neuropathy	E	*RP1L1*	NM_178857.6 (*RP1L1*): c.133C>T p.(Arg45Trp)	Heterozygous	NA	Occult macular dystrophy (OMIM#613587)

© 2025 Hong Kong Academy of Medicine Press | CC BY-NC-ND 4.0

89	Left retinoblastoma	H	*RB1*	NM_000321.2 (*RB1*): c.1399C>T p.(Arg467*), VAF 13%	VAF:13%	De novo	Retinoblastoma (OMIM#180200)
91	Bilateral macular dystrophy	B	*ABCA4*	NM_000350.3 (*ABCA4*): c.1804C>T p.(Arg602Trp)	Homozygous	In trans	Stargardt disease 1 (OMIM#248220)
92	Bilateral cataract and lattice degeneration of retina Stickler syndrome	B, C	*COL2A1*	NM_001844.5 (*COL2A1*): c.115C>T p.(Gln39*)	Heterozygous	Paternal	Stickler syndrome, type I (OMIM#108300)
93	Bilateral optic atrophy, progressive visual impairment, myoclonus, profound ataxia	E	*NEU1*	NM_000434.4 (*NEU1*): c.544A>G p.(Ser182Gly)	Homozygous	In trans	Sialidosis, type I (OMIM#256550)
95	Pierre Robin sequence, lattice degeneration of retina, mild hearing loss Stickler syndrome	B	*COL2A1*	NM_001844.5 (*COL2A1*): c.3109G>T p.(Glu1037*)	Heterozygous	Paternal	Stickler syndrome, type I (OMIM#108300)
97	Bilateral cataract	C	*CRYGD*	NM_006891.4 (*CRYGD*): c.474_475dup p.(Ala159Glyfs*10)	Heterozygous	Maternal	Cataract 4, multiple types (OMIM#115700)
101	Bilateral cataract	C	*GJA3*	NM_021954.4 (*GJA3*): c.184G>A	Heterozygous	De novo	Cataract 14, multiple types

© 2025 Hong Kong Academy of Medicine Press | CC BY-NC-ND 4.0

				p.(Glu62Lys)			(OMIM#601885)
102	Hearing loss with cochlear implant, retinitis pigmentosa Usher syndrome	B	*USH1C*	NM_153676.4 (*USH1C*): c.674+1G>T p.?	Homozygous	In trans	Usher syndrome, type 1C (OMIM#276904)
103	Hearing loss with retinitis pigmentosa, tunnel vision Usher syndrome	B	*USH2A*	NM_206933.3 (*USH2A*): c.5572+1G>A p.? NM_206933.3 (*USH2A*): c.8254G>A p.(Gly2752Arg)	Compound heterozygous	In trans	Usher syndrome, type 2A (OMIM#276901)
108	Retinitis pigmentosa	B	*CEP290*	NM_025114.4 (*CEP290*): c.6798G>A p.(Trp2266*)P Heterozygous NM_025114.4 (*CEP290*): c.1616del p.(Leu539*) LP-mat	Compound heterozygous	In trans	Senior-Loken syndrome 6 (OMIM#610189)
109	Cone-rod dystrophy	B	*RPGR*	NM_001034853.1 (*RPGR*): c.3166_3167del p.?	Hemizygous	Maternal	Cone-rod dystrophy, X-linked, 1 (OMIM# 304020)

© 2025 Hong Kong Academy of Medicine Press | CC BY-NC-ND 4.0

111	Poor night vision, retinitis pigmentosa, and maculopathy	B	*PDE6A*	NM_000440.3 (*PDE6A*): c.2198delinsGG p.(Gln733Argfs*9)	Homozygous	In trans	Retinitis pigmentosa 43 (OMIM#613810)
113	Bilateral severe hearing loss and retinitis pigmentosa Usher syndrome	B	*CLRN1*	NM_174878.3 (*CLRN1*): c.149C>A p.(Ser50*) NM_174878.3 (*CLRN1*): c.118T>C p.(Cys40Arg)	Compound heterozygous	In trans	Usher syndrome, type 3A (OMIM#276902)
115	Macular dystrophy	B	*RP1L1*	NM_178857.6 (*RP1L1*): c.133C>T p.(Arg45Trp)	Heterozygous	NA	Occult macular dystrophy (OMIM#613587)
117	Corneal granular dystrophy	I	*TGFBI*	Heterozygous NM_000358.3 (*TGFBI*): c.371G>A p.(Arg124His)	Heterozygous	NA	Corneal dystrophy, Avellino type (OMIM#607541)
118	Retinoschisis with partial retinal detachment	B	*RS1*	NM_000330.4 (*RS1*): c.99G>A p.(Trp33*)	Hemizygous	NA	Retinoschisis (OMIM#312700)

© 2025 Hong Kong Academy of Medicine Press | CC BY-NC-ND 4.0

119	Bietti crystalline corneoretinal dystrophy Hypercholesterolaemia	B	*CYP4V2*	NM_207352.4 (*CYP4V2*): c.1199G>A p.(Arg400His) NM_207352.4 (*CYP4V2*): c.802-8_810delinsGC p.?	Compound heterozygous	In trans	Bietti crystalline corneoretinal dystrophy (OMIM#210370)
120	Cleft palate and Pierre Robin sequence Stickler syndrome	B	*COL2A1*	NM_001844.5 (*COL2A1*): c.2818C>T p.(Arg940*)	Heterozygous	Incomplete	Stickler syndrome, type I (OMIM#108300)
121	Maculopathy with retinal flecks	B	*PRPH2*	NM_000322.5 (*PRPH2*): c.668T>A p.(Ile223Asn)	Heterozygous	NA	Macular dystrophy, vitelliform, 3 (OMIM#608161)
122	Total blindness and macular dystrophy	B	*PRPH2*	NM_000322.5 (*PRPH2*): c.309dup p.(Ile104Tyrfs*73)	Heterozygous	NA	Macular dystrophy, vitelliform, 3 (OMIM#608161)
123	Bilateral moderate hearing loss and retinitis pigmentosa Usher syndrome	B	*USH2A*	NM_206933.3 (*USH2A*): c.5572+1G>A p.? NM_206933.3 (*USH2A*): c.1655G>T p.(Cys552Phe)	Compound heterozygous	In trans	Usher syndrome, type 2A (OMIM#276901)

© 2025 Hong Kong Academy of Medicine Press | CC BY-NC-ND 4.0

125	Cortical blindness, porencephaly, global developmental delay, and epilepsy	E	*COL4A2*	NM_001846.4 (*COL4A2*): c.2821G>A p.(Gly941Arg)	Heterozygous	De novo	Brain small vessel disease 2 (OMIM#614483)
126	Syndromic: broad nasal tip, tapering fingers with prominent joints, broad thumbs, overlapping toes, congenital cataract, anterior segment features, and microphthalmia	A, C, D	*EP300*	NM_001429.4 (*EP300*): c.1765C>T p.(Gln589*)	Heterozygous	De novo	Rubinstein-Taybi syndrome 2 (OMIM#613684)
127	Oculocutaneous albinism	F	*TYR*	NM_000372.5 (*TYR*): c.119G>T p.(Trp400Leu) NM_000372.5 (*TYR*): c.446A>G p.(Tyr149Cys)	Compound heterozygous	In trans	Albinism, oculocutaneous, type IA (OMIM#203100)
129	Bilateral occult macular dystrophy	B	*RP1L1*	NM_178857.6 (*RP1L1*): c.133C>T p.(Arg45Trp)	Heterozygous	Maternal	Occult macular dystrophy (OMIM#613587)
130	Stickler syndrome	B	*COL2A1*	NM_0018844.5 (*COL2A1*): c.1310G>C	Heterozygous	NA	Stickler syndrome, type I

© 2025 Hong Kong Academy of Medicine Press | CC BY-NC-ND 4.0

	p.(Arg437Pro)	(OMIM#108300)

[*] Patient ID: Patients with revised diagnoses are highlighted in italic and underlined. These cases are categorised in this group because the diagnosis was made only after molecular testing, or because the confirmed molecular diagnosis is associated with additional features (eg, neurological involvement)

[†] Disease category: A=anterior segment dysgenesis; B=inherited retinal disorders; C=cataract/lens disorder; D=microphthalmia, anophthalmia, and coloboma [MAC] spectrum; E=neuro-ophthalmology; F=ocular albinism/oculocutaneous albinism; G=high myopia; H=ocular tumours; I=others

© 2025 Hong Kong Academy of Medicine Press | CC BY-NC-ND 4.0