Congenital eye disorders gene panel

Contact details

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Samples required

- 5ml venous blood in plastic EDTA bottles (>1ml from neonates)
- Prenatal testing must be arranged in advance, through a Clinical Genetics department if possible.
- Amniotic fluid or CV samples should be sent to Cytogenetics for dissecting and culturing, with instructions to forward the sample to the Regional Molecular Genetics laboratory for analysis
- A completed DNA request form should accompany all samples

Patient details

To facilitate accurate testing and reporting please provide patient demographic details (full name, date of birth, address and ethnic origin), details of any relevant family history and full contact details for the referring clinician

Introduction

Ocular conditions are highly heterogeneous and show considerable phenotypic overlap. 1 in 2,500 children in the UK are diagnosed as blind or severely visually impaired by the time they reach one year old. As many as half of these cases are likely to be inherited and remain undiagnosed due to the vast number of genes involved in these conditions. Many congenital eye disorders causing visual impairment or blindness at birth or progressive visual impairment also include syndromic conditions involving additional metabolic, developmental, physical or sensory abnormalities. Gene panels offer the enhanced probability of diagnosis as a very large number of genes can be interrogated.

Ocular birth defects include all inheritance modalities. Autosomal dominant and recessive diseases as well as X-linked dominant and recessive diseases are seen. These conditions can also be caused by *de novo* variants.

Referrals

- Patients presenting with a phenotype appropriate for the requested sub-panel
- Referrals will be accepted from clinical geneticists and consultants in ophthalmology.

Prenatal testing

Prenatal diagnosis may be offered as appropriate where pathogenic variants have been identified in accordance with expected inheritance pattern and where appropriate parental testing and counselling has been conducted.

Service offered

Analysis of coding regions and intron/exon boundaries of the genes listed in the sub-panels. If no clearly pathogenic variant is identified, re-analysis of the clinical exome data may be offered for other ocular sub-panels or other loci as appropriate.

Sub-panels:

- Eye malformations (includes ASD, cataract and expanded MAC panels)(EYEMALF)
- Microphthalmia, anophthalmia and coloboma (MAC) spectrum and aniridia
- Anterior segment dysgenesis (ASD) and glaucoma
- Retinal dystrophies (RETINAL)
- Ocular albinism, photophobia and nystagmus (ALB)
- Cataract, congenital, or lens malformations, congenital (CATARACT)
- Optic atrophy, childhood onset (OPTICATR)
- Eye movement disorders (EMD)

For gene lists see below.

Technical

Variant screening is carried out by next generation sequencing with library preparation using the Agilent focused clinical exome +1 kit followed by sequencing on the Illumina platforms. Data is analysed using an in-house pipeline with all pathogenic variants confirmed by Sanger sequencing.

Target reporting time

4 months for next generation sequencing screening in an index case. 4 weeks for familial testing.

Please contact the laboratory for urgent cases.

Congenital eye disorders gene panel

Eye malformations (EYEMALF):

ABCB6, ABHD12, ACTB, ACTG1, ADAMTS10, ADAMTS18, ADAMTSL4, AGBL1, AGK, AGPS, ALDH18A1, ALDH1A3, ATOH7, B3GLCT, BCOR, BEST1, BFSP1, BFSP2, BMP4, BMP7, C12ORF57, CBS, CC2D2A, CHD7, CHMP4B, CHRDL1, CHST6, CLDN19, COL18A1, COL4A1, COL8A2, CRIM1, CRYAA, CRYAB, CRYBA1, CRYBA4, CRYBB1, CRYBB2, CRYBB3, CRYGB, CRYGC, CRYGD, CRYGS, CTDP1, CYP1B1, CYP27A1, CYP51A1, DCN, DHCR7, DHX38, DPYD, EPG5, EPHA2, ERCC1, ERCC2, ERCC3, ERCC5, ERCC6, ERCC8, EYA1, FADD, FAM111A, FAM126A, FBN1, FNBP4, FOXC1, FOXE3, FOXL2, FRAS1, FREM1, FREM2, FTL, FYCO1, FZD5, GALK1, GALT, GCNT2, GDF3, GDF6, GFER, GJA1, GJA3, GJA8, GNPTG, GRIP1, GSN, HCCS, HMGB3, HMX1, HSF4, IGBP1, ITPA, ITPR1, JAM3, KAT6B, KERA, KMT2D, KRT12, KRT3, LAMB2, LCAT, LIM2, LMX1B, LRP2, LTBP2, MAB21L2, MAF, MAN2B1, MFRP, MIP, MIR184, MYH9, MYOC, NAA10, NF2, NHS, NOTCH2, OCRL, OPA3, OPTN, OTX2, P3H2, PAX2, PAX3, PAX6, PDE6D, PEX10, PEX11B, PEX12, PEX13, PEX14, PEX16, PEX19, PEX2, PEX26, PEX3, PEX5, PEX6, PIGL, PIKFYVE, PITX2, PITX3, POLR1C, POLR1D, PORCN, PQBP1, PRDM5, PRSS56, PTCH1, PXDN, RAB18, RAB3GAP1, RAB3GAP2, RARB, RAX, RBP4, RPGRIP1L, SALL1, SALL2, SALL4, SC5D, SCLT1, SEC23A, SEMA3E, SH3PXD2B, SHH, SIL1, SIX3, SIX6, SLC16A12, SLC2A1, SLC33A1, SLC38A8, SLC4A11, SLC4A4, SMCHD1, SMOC1, SOX2, SRD5A3, STRA6, TACSTD2, TBC1D20, TBC1D32, TBX22, TCOF1, TDRD7, TENM3, TFAP2A, TGFBI, TMEM67, TMEM98, TMX3, UBIAD1, VAX1, VIM, VSX1, VSX2, WDR36, WFS1, WRN, YAP1, ZEB1, ZEB2, ZIC2*

Microphthalmia, anophthalmia and coloboma spectrum and aniridia (MAC_v3):

ACTB, ACTG1, ALDH1A3, BCOR, C12ORF57, CHD7, COL4A1, FOXC1, FOXE3, FZD5, GJA8, ITPA, ITPR1, MAB21L2, NAA10, OTX2, PAX2, PAX6, PITX2, PITX3, RAB18, RAB3GAP1, RAB3GAP2, RARB, RAX, RBP4, SALL2, SALL4, SHH, SIX3, SMCHD1, SMOC1, SOX2, STRA6, TBC1D20, VAX1, VSX2, YAP1, ZEB2, ZIC2*

Anterior segment dysgenesis and glaucoma (ASD):

ADAMTS18, AGBL1, ALDH18A1, ATOH7, B3GLCT, BEST1, BMP7, CHRDL1, CHST6, COL4A1, COL8A2, CRIM1, CRYGC, CYP1B1, DCN, EYA1, FBN1, FOXC1, FOXE3, FOXL2, GJA1, GNPTG, GSN, KERA, KRT12, KRT3, LAMB2, LCAT, LMX1B, LTBP2, MIR184, MYOC, NOTCH2, OPTN, PAX3, PAX6, PEX2, PIKFYVE, PITX2, PITX3, PRDM5, PXDN, RAB18, RAB3GAP1, RAB3GAP2, SEC23A, SH3PXD2B, SIX3, SLC16A12, SLC38A8, SLC4A11, SLC4A4, TACSTD2, TBC1D20, TGFBI, UBIAD1, VSX1, WDR36, ZEB1

Retinal dystrophies (RETINAL_v3):

ABCA4, ABCC6, ABHD12, ACBD5, ACO2, ADAM9, ADAMTS18, ADGRA3, ADGRV1, AHI1, AIPL1, ALMS1, ARL13B, ARL2BP, ARL6, ATF6, ATOH7, B9D1, B9D2, BBIP1, BBS1, BBS10, BBS12, BBS2, BBS4, BBS5, BBS7, BBS9, BEST1, BMP7, C1QTNF5, C21orf2, C2ORF71, C5ORF42, C8ORF37, CA4, CABP4, CACNA1F, CACNA2D4, CAPN5, CC2D2A, CDH23, CDH3, CDHR1, CEP164, CEP290, CEP41, CERKL, CFH, CHM, CIB2, CLN3, CLRN1, CNGA1, CNGA3, CNGB1, CNGB3, CNNM4, COL11A1, COL2A1, COL4A1, COL9A1, CRB1, CRX, CSPP1, CYP4V2, DFNB31, DHDDS, DHX38, EFEMP1, ELOVL4, EMC1, EYS, FAM161A, FLVCR1, FSCN2, FZD4, GNAT1, GNAT2, GNPTG, GPR179, GRK1, GRM6, GUCA1A, GUCA1B, GUCY2D, HARS, HCCS, HESX1, HK1, HMCN1, IDH3B, IFT140, IFT172, IFT27, IMPDH1, IMPG1, IMPG2, INPP5E, INVS, IQCB1, ITM2B, JAG1, KCNJ13, KCNV2, KIAA1549, KIF11, KIF7, KIZ, KLHL7, LAMB2, LCA5, LRAT, LRIT3, LRP2, LRP5, LZTFL1, MAK, MERTK, MKKS, MKS1, MTTP, MVK, MYO7A, NDP, NEK2, NEUROD1, NMNAT1, NPHP1, NPHP3, NPHP4, NR2E3, NRL, NYX, OAT, OFD1, OPN1LW, OPN1MW*, OPN1SW, PANK2, PCDH15, PCYT1A, PDE6A, PDE6B, PDE6C, PDE6D, PDE6G, PDE6H, PDZD7, PEX1, PEX2, PEX7, PGK1, PHYH, PITPNM3, PLA2G5, PLK4, PMM2, PNPLA6, POC1B, PRCD, PROM1, PRPF3, PRPF31, PRPF4, PRPF6, PRPF8, PRPH2, RAB28, RAX2, RB1, RBP3, RBP4, RD3, RDH11, RDH12, RDH5, RGR, RGS9, RGS9BP, RHO, RIMS1, RLBP1, ROM1, RP1, RP1L1, RP2, RP9, RPE65, RPGR*, RPGRIP1, RPGRIP1L, RS1, SAG, SDCCAG8, SEMA4A, SLC24A1, SLC33A1, SLC38A8, SLC7A14, SNRNP200, SPATA7, TCTN1, TCTN2, TCTN3, TEAD1, TIMP3, TMEM138, TMEM216, TMEM231, TMEM237, TMEM67, TOPORS, TREX1, TRIM32, TRPM1, TSPAN12, TTC8, TTLL5, TTPA, TUB, TUBGCP4, TUBGCP6, TULP1, UNC119, USH1C, USH1G, USH2A, VCAN, VPS13B, WDPCP, WDR19, WFS1, ZNF423, ZNF513*

Ocular albinism, photophobia and nystagmus (ALB):

AP3B1, BLOC1S3, BLOC1S6, DTNBP1, GPR143, HPS1, HPS3, HPS4, HPS5, HPS6, MITF, OCA2, SLC45A2, TYR, TYRP1

Cataract, congenital, or lens malformations, congenital (CATARACT_v2):

ABHD12, ADAMTS10, ADAMTSL4, AGK, AGPS, ALDH18A1, BCOR, BEST1, BFSP1, BFSP2, CBS, CHMP4B, COL18A1, CRYAA, CRYAB, CRYBA1, CRYBA4, CRYBB1, CRYBB2, CRYBB3, CRYGB, CRYGC, CRYGD, CRYGS, CTDP1, CYP27A1, CYP51A1, DHCR7, DPYD, EPG5, EPHA2, ERCC2, ERCC3, ERCC5, ERCC6, ERCC8, FAM111A, FAM126A, FBN1, FTL, FYCO1, GALK1, GALT, GCNT2, GFER, GJA3, GJA8, HMX1, HSF4, JAM3, LIM2, MAF, MAN2B1, MIP, MYH9, NF2, NHS, OCRL, OPA3, OTX2, P3H2, PAX6, PEX10, PEX11B, PEX12, PEX13, PEX14, PEX16, PEX19, PEX26, PEX3, PEX5, PEX6, PITX3, PXDN, RAB18, RAB3GAP1, RAB3GAP2, SC5D, SEC23A, SIL1, SLC16A12, SLC2A1, SLC33A1, SLC4A4, SRD5A3, TBC1D20, TDRD7, WFS1, WRN, VIM

Optic atrophy, childhood onset (OPTICATR):

ALG3, C12ORF65, KIF7, MFN2, NR2F1, OPA1, OPA3, RAB3GAP1, SPG7, TBC1D20, TIMM8A, TMEM126A, WFS1

Eye movement disorders (EMD_v2):

CHN1, COL25A1, DCC, FRMD7, HOXA1, HOXB1, KIF21A, MAFB, PHOX2A, ROBO3, SALL1, SALL4, TUBB2B, TUBB3*

*Genes marked with an asterisk have low (<90%) horizontal coverage due to sequence context and/or the presence of highly homologous regions in the genome.