EYE OPHTHALRESEARCH TEST RESULTS

KIT ID: SAMPLE

Ophtalmology Test

Introduction

The Ophthalmology Test is based on Whole Genome Sequencing Test. As such, it analyzes all Common and Rare Variants associated with Eye Diseases, including retinal disorders, blindness, glaucoma and refractive errors. Along with environmental factors, Genetics plays a key role in the regulation of Eye Diseases. - More than 400 genes analyzed - 100% genomic regions covered - Intragenic and intergenic regions analyzed - All variants reported

In our analysis, we did not find any pathogenic variants.

Genes/Locations included in report

Genes in which variants of interest have been detected are listed in bold

AASS, ABCA4, ABCB6, ABHD12, ACO2, ADAM9, ***ADAMTS10 (1)****,* ***ADAMTS17 (1)****, ADAMTS18, ADAMTSL4, ADGRV1, ADIPOR1, AGBL5, AGK, AHI1, AIPL1, ALDH18A1, ALDH1A3, ALMS1, ANTXR1, AP3B1, APTX, ARHGEF18, ARL13B, ARL2BP, ARL6, ARMC9, ASPH, ATF6, ATOH7, B9D1, B9D2, BBIP1, BBS1, BBS10, BBS12, BBS2, BBS4, BBS5, BBS7, BBS9, BCOR, BEST1, BFSP1, BFSP2, BLOC1S3, BLOC1S6, BMP4, BMP7, C10ORF11, C10ORF2, C12ORF65, C1QTNF5, C21ORF2, C2ORF71, C5ORF42, C8ORF37, CA4, CABP4, CACNA1F, CACNA2D4, CAPN5, CBS, CC2D2A,* ***CDH23 (1)****, CDH3,* ***CDHR1 (1)****, CEP104, CEP120, CEP164,* ***CEP290 (1)****, CEP41, CEP78, CERKL,* ***CHD7 (1)****, CHM, CHMP4B, CHN1, CHRDL1,* ***CHST6 (1)****, CIB2, CISD2, CLN3, CLRN1, CNGA1, CNGA3 ,* ***CNGB1 (1)****, CNGB3, CNNM4,* ***CNTNAP2 (1)****, COL11A1, COL11A2, COL17A1, COL18A1, COL2A1, COL4A1, COL5A1, COL8A2, COL9A1, COL9A2, COL9A3, COX7B, CRB1,* ***CRX (1)****, CRYAA, CRYAB, CRYBA1, CRYBA4, CRYBB1, CRYBB2, CRYBB3, CRYGC, CRYGD, CRYGS, CSPP1, CTC1, CTDP1, CTNNA1, CTNNB1, CWC27,* ***CYP1B1 (1)****, CYP27A1,* ***CYP4V2 (1)****, DCN, DFNB31, DHDDS, DHX38, DRAM2, DTHD1, DTNBP1, EFEMP1, ELOVL4, EMC1, EPHA2, ERCC2, ERCC5,* ***ERCC6 (1)****, ERCC8,* ***EYA1 (1)****, EYS, FAM126A, FAM161A, FBN1, FDXR,* ***FLVCR1 (1)****, FOXC1, FOXE3, FOXL2,* ***FRAS1 (1)****,* ***FREM1 (1)****, FREM2, FRMD7, FTL, FYCO1,* ***FZD4 (1)****, GALE, GALK1,* ***GALT (1)****, GCNT2, GJA1, GJA3, GJA8, GNAT1, GNAT2,* ***GNB3 (1)****, GNPTG, GPR143, GPR179, GRIP1, GRM6, GSN, GUCA1A, GUCY2D, HARS, HCCS, HESX1, HGSNAT, HK1, HMX1, HPS1, HPS3,* ***HPS4 (1)****, HPS5, HPS6, HSF4, IDH3B, IFT140, IFT172, IFT81, IMPDH1, IMPG1, IMPG2, INPP5E, INVS, IQCB1, JAG1, KCNJ13, KCNV2, KERA, KIAA0556, KIAA0586, KIAA0753, KIF11, KIF21A, KIF7, KIZ, KLHL7, KRT12, KRT3,* ***LCA5 (1)****, LCAT, LIM2,* ***LMX1B (1)****, LOXHD1, LRAT, LRIT3,* ***LRP2 (1)****, LRP5, LTBP2 , LYST, LZTFL1, MAB21L2, MAF, MAK, MC1R, MERTK, MFN2, MFRP, MFSD8, MIP, MITF, MKKS, MKS1, MLPH, MMACHC, MTTP, MVK, MYH9, MYO5A, MYO7A, MYOC, NAA10, NDP,* ***NDUFS1 (1)****, NEK2,* ***NF2 (1)****, NHS, NMNAT1, NPHP1, NPHP3, NPHP4,* ***NR2E3 (1)****, NR2F1, NRL, NYX,* ***OAT (1)****, OCA2, OCRL, OFD1, OPA1,* ***OPA3 (1)****, OPTN, OTX2, OVOL2, P3H2, PANK2, PAX2, PAX6,* ***PCDH15 (1)****, PCYT1A,* ***PDE6A (1)****,* ***PDE6B (1)****, PDE6C, PDE6D, PDE6G, PDE6H, PDZD7,* ***PEX1 (1)****, PEX10, PEX11B, PEX12, PEX13, PEX14, PEX16, PEX19, PEX2, PEX26, PEX3, PEX5, PEX6, PEX7, PHOX2A,* ***PHYH (1)****, PIKFYVE, PITPNM3, PITX2, PITX3, PLA2G5, PNPLA6, POC1B, POLG, PORCN, PQBP1, PRCD, PRDM13, PRDM5, PRKCG, PROM1, PRPF3, PRPF31, PRPF4, PRPF6, PRPF8, PRPH2, PRPS1, PRSS56, PXDN, RAB27A, RAB28,* ***RAB3GAP1 (1)****, RARB, RAX, RAX2, RBP3, RBP4,* ***RD3 (1)****, RDH11, RDH12, RDH5, RECQL4, REEP6, RGR, RGS9, RGS9BP, RHO, RIMS1, RLBP1, ROBO3, ROM1, RP1, RP1L1, RP2, RPE65, RPGR, RPGRIP1, RPGRIP1L, RRM2B, RS1, RTN4IP1, SAG, SALL4, SAMD11, SDCCAG8, SEMA4A, SETX, SHH, SIL1, SIX3, SIX6, SLC16A12, SLC24A1, SLC24A5, SLC25A4, SLC25A46, SLC33A1, SLC38A8, SLC45A2, SLC4A11, SLC52A2, SLC7A14, SMCHD1, SMOC1,* ***SNRNP200 (1)****, SNX10, SOX2, SPATA7, SPG7, SPP2, STRA6, SUOX, TACSTD2, TBK1,* ***TCF4 (1)****, TCTN1, TCTN2, TCTN3, TDRD7, TEAD1, TEK, TENM3, TFAP2A, TGFBI, TIMM8A,* ***TIMP3 (1)****, TK2, TMEM107, TMEM126A, TMEM138, TMEM216, TMEM231, TMEM237, TMEM67, TMEM70, TOPORS, TRAF3IP1, TREX1, TRIM32, TRPM1, TSPAN12, TTC21B, TTC8, TTLL5, TTPA, TUB, TUBB3, TULP1, TYMP, TYR, TYRP1, UBIAD1, USH1C, USH1G, USH2A, VCAN, VIM, VPS13B, VSX2, WDPCP, WDR19, WDR36, WFS1, WRN, ZEB1, ZIC2, ZNF408, ZNF423, ZNF469, ZNF513*

Clinical Variants Found:

#	Gene/Loc	Chr: Pos	rsID, Variant Description	Variation ID	Phenotype Name	Zygosity	Genomic Variant	Allele Frequency	Significance	Review Status
	ADAMTS17	15:100513587	rs11277519 - NM_139057.4(ADAMTS17):c.*1014_*1019del	315201	• Weill-Marchesani syndrome 4	HET	CTGGGCT>C		conflicting interpretations of pathogenicity	★
	CDH23	10:73157033	rs71012280 - NM_022124.6(CDH23):c.-45_-41AGGCG[4]	300394	• Retinitis pigmentosa-deafness syndrome • CDH23-Related Disorders • Nonsyndromic Hearing Loss	HOM	C>CCGAGG		conflicting interpretations of pathogenicity	★
	CEP290 Rare	chr12:88533296	rs373913704 - NM_025114.3(CEP290):c.226G>A (p.Ala76Thr)	166841	• Nephronophthisis • Joubert syndrome • Meckel-Gruber syndrome	HET	C>T	0.00058	conflicting interpretations of pathogenicity	★
	CYP1B1	chr2:38301847	rs57865060 - NM_000104.3(CYP1B1):c.685G>A (p.Glu229Lys)	68467	• Congenital ocular coloboma • Primary congenital glaucoma • Glaucoma 3	HET	C>T	0.01038	conflicting interpretations of pathogenicity	★
	GALT	chr9:34649442	rs2070074 - NM_000155.4(GALT):c.940A>G (p.Asn314Asp)	3613	• GALT POLYMORPHISM (DUARTE	HET	A>G	0.07288	conflicting interpretations of pathogenicity	★
	PCDH15 Rare	chr10:56106173	rs34164469 - NM_033056.4(PCDH15):c.546A>G (p.Gly182=)	46501	• Retinitis pigmentosa-deafness syndrome • Nonsyndromic Hearing Loss	HET	T>C	0.00719	conflicting interpretations of pathogenicity	★
	PEX1	7:92129161	rs5885806 - NM_000466.3(PEX1):c.2584-10del	360922	• Peroxisome biogenesis disorder 1A (Zellweger)	HET	CA>C		conflicting interpretations of pathogenicity	★

#	Gene/Loc	Chr: Pos	rsID, Variant Description	Variation ID	Phenotype Name	Zygosity	Genomic Variant	Allele Frequency	Significance	Review Status
	PHYH Rare	chr10:13325784	rs62619919 - NM_006214.4(PHYH):c.734G>A (p.Arg245Gln)	198539	• Nonsyndromic cleft lip palate • Phytanic acid storage disease	HET	C>T	0.00539	conflicting interpretations of pathogenicity	★
	RAB3GAP1 Rare	chr2:135920394	rs61748693 - NM_012233.3(RAB3GAP1):c.2463C>T (p.Phe821=)	130068	• Warburg micro syndrome	HET	C>T	0.00419	conflicting interpretations of pathogenicity	★
	ADAMTS10	19:8645320	rs34057037 - NM_030957.4(ADAMTS10):c.*456del	330567	• Weill-Marchesani syndrome	HET	AC>A		uncertain significance	★
	CDHR1	chr10:85956268	rs12781048 - NM_033100.4(CDHR1):c.159C>A (p.His53Gln)	301212	• Cone-Rod Dystrophy	HET	C>A	0.01937	uncertain significance	★
1	*CHD7*	chr8:61690321	rs4738824 - NM_017780.4(CHD7):c.1666-3238A>G	2030	• Scoliosis	HOM	A>G	0.86062	uncertain significance	
	CHST6	16:75510458	rs36092135 - NM_021615.5(CHST6):c.*2080del	320555	• Macular corneal dystrophy Type I	HOM	CA>C		uncertain significance	★
	CNGB1 Rare	chr16:58001086	rs61997250 - NM_001297.5(CNGB1):c.105G>A (p.Ala35=)	320114	• Retinitis Pigmentosa	HET	C>T	0.00819	uncertain significance	★
	CRX	19:48343960	rs60558029 - NM_000554.6(CRX):c.*754_*756dup	329720	• Leber congenital amaurosis • Cone-Rod Dystrophy	HET	C>CTTTT		uncertain significance	★
	CYP4V2	4:187132852	rs58524374 - NM_207352.4(CYP4V2):c.*1059_*1060CA[5]	348346	• Bietti crystalline corneoretinal dystrophy • Corneal Dystrophy	HOM	T>TACAC		uncertain significance	★
	EYA1	8:72274390	rs35320129 - NM_172059.5(EYA1):c.34-5669_34-5668dup	363682	• Otofaciocervical syndrome 1 • Branchiootorenal Spectrum Disorders	HET	C>CTT		uncertain significance	★

#	Gene/Loc	Chr: Pos	rsID, Variant Description	Variation ID	Phenotype Name	Zygosity	Genomic Variant	Allele Frequency	Significance	Review Status
	FLVCR1	1:213069469	rs549002753 - NM_014053.4(FLVCR1):c.*838_*839CT[2]	295342	• Posterior column ataxia with retinitis pigmentosa	HET	ACT>A		uncertain significance	★
	FRAS1 Rare	chr4:79173616	rs147709711 - NM_025074.7(FRAS1):c.380C>G (p.Pro127Arg)	349657	• Cryptophthalmos syndrome	HET	C>G	0.00439	uncertain significance	★
	FREM1 Rare	chr9:14869124	rs560738143 - NM_144966.5(FREM1):c.-149A>G	366183	• Marles Greenberg Persaud syndrome	HET	T>C	0.0006	uncertain significance	★
	FZD4	11:86658243	rs34325935 - NM_012193.4(FZD4):c.*3909_*3912TTTG[7]	306349	• Familial exudative vitreoretinopathy	HOM	TCAAA>T		uncertain significance	★
	HPS4	chr22:26847968	rs56271395 - NM_022081.5(HPS4):c.*1231C>T	340984	• Hermansky-Pudlak syndrome	HET	G>A		uncertain significance	★
	LCA5	chr6:80195421	rs16890805 - NM_001122769.3(LCA5):c.*1300G>A	358073	• Leber congenital amaurosis	HET	C>T	0.02416	uncertain significance	★
	LMX1B	9:129460116	rs59836255 - NM_001174146.1(LMX1B):c.*1387_*1391TGTTT[8]	364924	• Nail-patella syndrome	HET	CTGTTTTGTTTTGTTT>C		uncertain significance	★
	LRP2	2:169984043	rs3083240 - NM_004525.3(LRP2):c.*1128_*1129dup	332047	• Donnai Barrow syndrome	HET	T>TAA		uncertain significance	★
	NDUFS1	2:207014657	rs568965659 - NM_005006.7(NDUFS1):c.154-10_154-9del	333789	• Leigh syndrome • Mitochondrial complex I deficiency	HET	TAA>T		uncertain significance	★
	NF2	22:30092055	rs886057354 - NM_000268.4(NF2):c.*1287dup	341104	• Neurofibromatosis	HET	C>CT		uncertain significance	★
	NR2E3 Rare	chr15:72102945	rs138513681 - NM_014249.4(NR2E3):c.-139G>A	317001	• Enhanced s-cone syndrome • Retinitis Pigmentosa	HET	G>A	0.00399	uncertain significance	★

#	Gene/Loc	Chr: Pos	rsID, Variant Description	Variation ID	Phenotype Name	Zygosity	Genomic Variant	Allele Frequency	Significance	Review Status
	OAT Rare	chr10:126107434	rs552799531 - NM_000274.3(OAT):c.-30+8C>T	299177	• Ornithine aminotransferase deficiency	HET	G>A	0.0012	uncertain significance	★
	OPA3	19:46052048	rs58537694 - NM_025136.4(OPA3):c.*4696_*4699ATAA[9]	329599	• 3-Methylglutaconic aciduria type 3 • Optic Atrophy	HET	C>CTTATTTAT		uncertain significance	★
	PDE6A	5:149238389	rs57328066 - NM_000440.3(PDE6A):c.*2068del	351953	• Retinitis Pigmentosa	HET	TC>T		uncertain significance	★
	PDE6B	4:664028	rs374413250 - NM_000283.3(PDE6B):c.*153dup	349404	• Congenital Stationary Night Blindness	HOM	A>AT		uncertain significance	★
	RD3	1:211665390	rs34485370 - NM_001164688.1(RD3):c.-336_-335AC[21]	295276	• Leber congenital amaurosis	HET	GGT>G		uncertain significance	★
	SNRNP200 Rare	chr2:96940419	rs557818805 - NM_014014.5(SNRNP200):c.*331G>C	337518	• Retinitis Pigmentosa	HET	C>G	0.0002	uncertain significance	★
	TCF4	18:52891395	rs66807288 - NM_001083962.2(TCF4):c.*3870del	327252	• Pitt-Hopkins syndrome	HET	CT>C		uncertain significance	★
	TIMP3	22:33256900	rs766674644 - NM_003490.4(SYN3):c.711+4000_711+4001del	341366	• Pseudoinflammatory fundus dystrophy	HET	GTT>G		uncertain significance	★

Informational Variants Found:

#	Gene/Loc	Chr: Pos	rsID, Variant Description	Variation ID	Phenotype Name	Zygosity	Genomic Variant	Allele Frequency	Significance	Review Status
1	*CNTNAP2*	chr7:146489606	rs7794745 - NM_014141.6(CNTNAP2):c.208+18133A>T	5492	• Autism 15	HET	A>T	0.50539	risk factor	
2	*ERCC6*	chr10:50747539	rs3793784 - NM_001277059.1(ERCC6):c.-76C>G	1709	• LUNG CANCER	HET	G>C	0.23782	risk factor	
	GNB3	chr12:6954875	rs5443 - NM_002075.4(GNB3):c.825C>T (p.Ser275=)	226004	• sildenafil response - Efficacy	HET	C>T	0.49221	drug response	★★★

Individual Clinical Variant Interpretations:

#	
1	**rs4738824 - NM_017780.4(CHD7):c.1666-3238A>G** This variant, formerly titled SCOLIOSIS, IDIOPATHIC, SUSCEPTIBILITY TO, 3, has been reclassified based on the findings of Tilley et al. (2013). To search for genes underlying susceptibility to idiopathic scoliosis (see IS3, 608765), Gao et al. (2007) ascertained a cohort of 52 families and conducted a study by genomewide scans, which produced evidence of linkage in association with 8q12 loci (multipoint lod = 2.77; p = 0.0028). Further mapping in the region showed significant evidence of disease-associated haplotypes centering over exons 2 through 4 of the CHD7 gene, which is associated with the CHARGE syndrome of multiple developmental anomalies. In 25 affected probands with idiopathic scoliosis (see IS3, 608765) and 44 parental controls, Gao et al. (2007) identified a single-nucleotide polymorphism, SNP rs4738824, an A-to-G change in intron 2 of the CHD7 gene that was predicted to disrupt a caudal-type (cdx) transcription factor binding site. The A nucleotide of this SNP appears to be perfectly conserved across 9 vertebrate species. In the 27 remaining families in the study, Gao et al. (2007) found significant overtransmission of the G allele, which was predicted to disrupt a caudal-type (cdx) transcription factor binding site, to affected offspring (p = 0.005). Tilley et al. (2013) performed model-independent linkage analysis and tests of association for 22 single-nucleotide polymorphisms in the CHD7 gene in 244 families of European descent with familial idiopathic scoliosis. Linkage analysis identified 3 marginally significant results. However, their results were not significant for tests of association to the CHD7 gene (p less than 0.01). In addition, no significant results (p less than 0.01) were found from a metaanalysis of the results from the tests of association from their sample and that of Gao et al. (2007). PubMed PMID: 23883829 PubMed PMID: 17436250

Individual Informational Variant Interpretations:

#	
1	**rs7794745 - NM_014141.6(CNTNAP2):c.208+18133A>T** In 2 independent family-based samples, Arking et al. (2008) identified a common variant in the CNTNAP2 gene, rs7794745, that was associated with increased risk for autism (AUTS15; 612100). This SNP resides in intron 2 of the CNTNAP2 gene. In the combined sample, overall transmission frequency of the T allele to affected children (tau = 0.55, p less than 7.35 x 10(05)) was significantly greater from mothers (tau = 0.61) than from fathers (tau = 0.53), and this parent-of-origin difference was significant (P less than 0.001). PubMed PMID: 18179894
2	**rs3793784 - NM_001277059.1(ERCC6):c.-76C>G** In a cohort of 460 ARMD cases and 269 age-matched controls and 57 archived ARMD cases and 18 age-matched non-ARMD controls, Tuo et al. (2006) found that a -6530C-G SNP (rs3793784) in the 5-prime flanking region of the ERCC6 gene was associated with ARMD5 susceptibility (613761), both independently and through interaction with an intronic G-C SNP in the CFH gene (rs380390; 134370.0008) previously reported to be highly associated with ARMD. A disease odds ratio of 23 was conferred by homozygosity for risk alleles at both ERCC6 and CFH (G allele and C allele, respectively) compared to homozygosity for nonrisk alleles. Tuo et al. (2006) suggested that the strong ARMD predisposition conferred by the ERCC6 and CFH SNPs may result from biologic epistasis. In functional studies on the -6530C-G SNP, Tuo et al. (2006) found that the SNP conferred a distinct change in regulation of gene expression in vitro and in vivo, with enhanced expression associated with the G allele. Lin et al. (2008) found that the -6530C allele has about 2-fold decreased transcriptional activity as well as decreased binding affinity of nuclear proteins compared to the G allele. In a case-control study of 1,000 Chinese patients with various types of lung cancer (see 211980) and 1,000 Chinese controls, those with the CC genotype had a 1.76-fold increased risk of disease compared to those with the CG or GG genotypes (p = 10(-9)). The C allele also interacted with smoking to intensify lung cancer risk, yielding an odds ratio of 9.0 for developing cancer among heavy smokers. PubMed PMID: 16754848 PubMed PMID: 17854076

In our analysis, we did not find any related conditions

Glossary

Symbol		Description
AD	Autosomal dominant	One mutated copy of the gene in each cell is sufficient for a person to be affected by an autosomal dominant disorder. In some cases, an affected person inherits the condition from an affected parent. In others, the condition may result from a new mutation in the gene and occur in people with no history of the disorder in their family.
AR	Autosomal recessive	In autosomal recessive inheritance, both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition. Autosomal recessive disorders are typically not seen in every generation of an affected family.
X-linked dominant	X-linked	Dominant X-linked dominant disorders are caused by mutations in genes on the X chromosome, one of the two sex chromosomes in each cell. In one of the two sex chromosomes in each cell. In females (who have two X chromosomes), a mutation in one of the two copies of the gene in each cell is sufficient to cause the disorder. In males (who have only one X chromosome), a mutation in the only copy of the gene in each cell causes the disorder. In most cases, males experience more severe symptoms of the disorder than females. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons (no male-to-male transmission).
Y-linked	Y-linked	A condition is considered Y-linked if the mutated gene that causes the disorder is located on the Y chromosome, one of the two sex chromosomes in each of a male's cells. Because only males have a Y chromosome, in Y-linked inheritance, a mutation can only be passed from father to son.
Mitochondrial	Mitochondrial	Mitochondrial inheritance, also known as maternal inheritance, applies to genes in mitochondrial DNA. Mitochondria, which are structures in each cell that convert molecules into energy, each contain a small amount of DNA. Because only egg cells contribute mitochondria to the developing embryo, only females can pass on mitochondrial mutations to their children. Conditions resulting from mutations in mitochondrial DNA can appear in every generation of a family and can affect both males and females, but fathers do not pass these disorders to their daughters or sons.
Pathogenic		This variant directly contributes to the development of disease. Some pathogenic variants may not be fully penetrant. In the case of recessive or X-linked conditions, a single pathogenic variant may not be sufficient to cause disease on its own. Additional evidence is not expected to alter the classification of this variant.
Likely Pathogenic		There is a high likelihood (greater than 90% certainty) that this variant is disease-causing. Additional evidence is expected to confirm this assertion of pathogenicity, but there is a small chance that new evidence may demonstrate that this variant does not have clinical significance.
VUS	Variant Uncertain significance	There is not enough information at this time to support a more definitive classification of this variant.
Phenotype Name		Phenotype represents the observable characteristics or traits of an organism that are produced by the interaction of the genotype and the environment : the physical expression of one or more genes.
Zygosity		Zygosity refers to the similarity of alleles for a trait in an organism. If both alleles are the same, the organism is homozygous for the trait. If both alleles are different, the organism is heterozygous for that trait. If one allele is missing, it is hemizygous, and, if both alleles are missing, it is nullizygous

Symbol		Description
Allele Frequency		Allele frequency is a measure of the relative frequency of an allele on a genetic locus in a specific position and it is expressed as a proportion or a percentage. Population genetics studies the different "forces" that might lead to changes in the distribution and frequencies of alleles - in other words, to evolution. Besides selection, these forces include genetic drift, mutation, and migration. Based on their frequency, the variants can be classified in rare variants and common genetic variants. Rare variants are alternative forms of a gene that are present with a minor allele frequency (MAF) of less than 1%. As a general principle, rare variants are more likely to cause rare diseases while common variants are more likely to increase the risks of genetic and complex diseases.
Significance		Significance refers to the standard term used by ClinVar, the internationally recognized database on which this report is based, to classify the types of variants. As the database is a clinical database, the information is clinical and based on an authoritative source when available. The Significance section includes the following standard terms to classify the variants: • **Pathogenic**: A Pathogenic is classified as such if this variant directly contributes to the development of disease. Some pathogenic variants may not be fully penetrant. In the case of recessive or X-linked conditions, a single pathogenic variant may not be sufficient to cause disease on its own. Additional evidence is not expected to alter the classification of this variant. • **Likely Pathogenic**: A Likely Pathogenic variant is classified as such if there is a high likelihood (greater than 90% certainty) that this variant is disease-causing. Additional evidence is expected to confirm this assertion of pathogenicity, but there is a small chance that new evidence may demonstrate that this variant does not have clinical significance. • **Conflicting Interpretations of Pathogenicity**: A Conflicting Interpretations of Pathogenecitity variant is classified as such if it is submitted from a scientific consortium, where groups within the consortium have conflicting interpretations of a variant but provide a single submission to ClinVar. • **Variant of Unknown Significance**: A Variant of Unknown Significance is classified as such if it is there is not enough information at this time to support a more definitive classification of this variant. • **Drug response**: A Drug response variant is classified as such if it represents a complex phenotype that emerges from the interplay of drug-specific genetics, human body, and environmental factors. • **Association**: An association variant is classified as such if there are one or more genotypes within a population co-occur with a phenotypic trait more often than would be expected by chance occurrence.
Review Status		ClinVar reports the level of review supporting the assertion of clinical significance for the variation as review status. Stars provide a graphical representation of the aggregate review status on web pages. Table 1 provides definitions of each review status and the corresponding number of stars. Review status is reported in text format in ClinVar's products available by FTP. A higher number of gold stars corresponds to higher review status. If you wish to get more information about that, please visit ClinVar at the following link: https://www.ncbi.nlm.nih.gov/clinvar/docs/review_status/

Methods

Versions

VCF Version: 09kXFFjmhLfYAXKNq_61TAX9yN2hXhxj
Clinvar Database Version: QoqCB67VTISXJBo0M_5ZtdenJ9F4gGG0

Extraction

Before sequencing, DNA extraction and library preparation processes were carried-out by automated liquid handling robots. Sequencing was completed using the NovaSeq 6000 instrument (Illumina).

The Nextera DNA Flex (Illumina) library was used during sequencing.

Analysis

Primary and secondary analysis was performed on the Illumina DRAGEN platform. Our secondary analysis extends the GATK 'best practices' pipeline. This includes Variant Quality Score Recalibration

It is important to note that applying a filter will not remove any data from the VCF file; it will just annotate the "FILTER" column. Variants with the "PASS" annotation are considered high quality and may, therefore, be used for advanced downstream analysis.

Sequence data is primarily aligned to the GATK GRCh37 reference genome and mitochondria is aligned to the Revised Cambridge Reference Sequence (NC_012920.1). Additional references may have been requested though tertiary analysis is not conducted on variant calls using references other than GRCh37.

Limitations

Test results are not interpretations. All variants reported in the genes included in the panel are reported.

Rare polymorphisms may lead to false-negative or false-positive results.

Due to limited read length and other contributing technical limitations, repeat expansions (e.g. in the Huntington gene, the SCA-genes, the myotonic dystrophy repeat region, and other similar regions) cannot be assessed with the applied method

Disclaimer

Any preparation and processing of a sample from saliva collection kit to Dante Labs by a customer is assumed to belong to the email used by the customer at the moment of kit registration on the Dante Labs Genome Manager platform before the shipment of the specimen to the laboratory.

The analysis and reporting conducted by Dante Labs are based on information from one or more published third-party scientific and medical studies.

Because of scientific and medical information changes over time, your risk assessment for one or more of the conditions contained within this report may also change over time. For example, opinions differ on the importance and relative weights given to genetic factors. Also, epidemiological data isn't available for some conditions, and this report may not be able to provide definitive information about the severity of a particular condition. We recommend asking your healthcare provider to correctly interpret them. Therefore, this report may not be 100% accurate (e.g., new research could mean different results) and may not predict actual results or outcomes.

This test has not been cleared or approved by the U.S. Food and Drug Administration (FDA). The US Food and Drug Administration (FDA) has determined that clearance or approval of this method is not necessary and thus neither have been obtained.

Contact

Please contact contact@dantelabs.com for more information on the contents of this report, our analysis methodology, and the limitations of this process.