OMNIHEALTH DIAGNOSTICS

Herediatry Eye Disorders Risk Panel

Patient		Specimen		Ordering Physician	
First Name:	John	Specimen Type:	Buccal Swab	Physician:	Test Doctor
Last name:	Doe	Collection Date:	04-01-2023	Institution:	Test Facility
Date of Birth:	09-31-9999	Received Date:	04-11-2023	Reported Date:	04-18-2023
Gender:	Male	Panel Coverage :	96.48%	Ref Accession:	N/A
Accession ID:	EYE04172023	Average Read Depth:	211x		

Test Result:

Pathogenic / Likely Pathogenic variant detected on MYOC gene.

Gene & Transcript	Variant	Inheritance	Disorder or Phenotype	Criteria	Classification
MYOC NM_000261.2	c.1102C>T	Autosomal dominant Heterozygous	Constitutional mismatch repair deficiency syndrome	PVS1, PM2, PP1 and PP4	Pathogenic

Location	Allele State	Allelic Read Depths
Exon 3	Heterozygous	Ref(GA): 220, Alt(-): 52, VAF: 19.12%

Genomic Position	Variant Frequency
Chr.1-245757381	0.00004588 and 0.013 in Ashkenazi Jews.

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Gene info 	MYOC NM_000261.2
Variant Info 	The Variant is found at Chr.1-245757381 location with a rs74315329 variant c.1102C>T change on the patient's MYOC
Variant interpretation 	The rs74315329 variant, which is also known as the Gln368Ter variant in the MYOC gene, is located in the exon 3 of the MYOC gene. Specifically, the variant results in a C to T substitution at nucleotide position 1102 of the MYOC coding sequence, which causes a premature stop codon in exon 3. Exon 3 encodes for a part of the olfactomedin-like domain of the myocilin protein, which is involved in the regulation of intraocular pressure and is mutated in glaucoma. This variant results in a premature stop codon and is one of the most common pathogenic variants associated with juvenile-onset and late-onset primary open-angle glaucoma (POAG). Individuals who inherit two copies of this variant (homozygous) have a high risk of developing glaucoma, while those who inherit one copy (heterozygous) have a lower risk. Hence it is considered a pathogenic variant.
Inheritance 	Autosomal dominant Heterozygous
ACMG-Classification	Pathogenic (PVS1, PM2, PP1 and PP4)
Gene & Disorder or Phenotype	Constitutional mismatch repair deficiency syndrome
What's next 	Correlate the findings with clinical symptoms, biochemical profile and family history whilst closely monitoring the subject with periodical visits.Genetic counseling is recommended.

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Test Methodology

Hereditary Eye Disease Risk Panel Screens 83 genes on the Next Generation Sequencing (NGS) technology using the targeted gene enrichment chemistry on the IIlumina® MiniSeq platform. Genomic DNA extracted from Buccal swabs (Dry and Wet) are tagemented and enriched for regions of interest using probes specific for each region specified in the BED (Browser Extensible Data) file. Positive (www.coriell.org) and Negative controls are included with each machine run to ensure the accuracy of amplicon preparation alongside targeted sequencing on coding regions and intronic/exonic boundaries of interest and precise finding of the variant on the positive control and negative control respectively. Exclusions from analysis are listed below Sequences obtained are then aligned against a human reference genome and variants such as SNVs (Small Nucleotide Variants) and Indels (Insertions and Deletions) are noted. For a detailed list of regions covered and comprehensive statistics by Elite Clinical Lab's Hereditary Eye Disease Risk Panel, please contact us on Email: 12345@omnihealthdx.com

Computational analysis and variant calling were performed by Elite Clinical Lab (www.eliteclinicallab.com). Briefly, reads from output were aligned to the human reference genome (GRCh37) using the Burrows-Wheeler Aligner (BWA). Variants to the reference were called using the Genomic Analysis Tool Kit (GATK). The variants were annotated and filtered using the Elite Clinical Lab analysis workflow implementing the ACMG guidelines for interpretation of sequence variants. This includes comparison against the gnomAD population catalog of variants in 123,136 exomes, the 1000 Genomes Project Consortium's publication of 2,500 genomes, the NCBI-ClinVar database of clinical assertions on variant's pathogenicity and multiple lines of computational evidence on conservation and functional impact. The following databases and insilico algorithms are used to annotate and evaluate the impact of the variant in the context of human disease: 1000 genomes, gnomAD, ClinVar, OMIM, dbSNP, NCIB Ref Seq Genes, ExAC Gene Constraints, VS-SIFT, VS PolyPhen2, PhyloP, GERP+, GeneSplicer, Max EntScan, NNSplice, PWM Splice Predictor. Analysis was reported using the HGVS nomenclature (www.hgvs.org/mutnomen)as implemented by custom transcript annotation algorithm. Only variants with an end ACMG classification of "Pathogenic" or "Likely Pathogenic" are reported and VUS/Benign/Likely Benign variants are not reported. Classification of pathogenicity is consistently updated by the National Institutes of Health and the information found within this report is consistent with the current knowledge base as the knowledge base changes, so may clinical interpretation of variants. All reports are reviewed prior to release by either Elite Clinical Lab's Technical Supervisor or the General Supervisor.

Genes Evaluated

FOXC1, ALDH7A1, ATXN7, CACNA1A, CDH23, CDKL5, CFH, CHD2, CLRN, CNGA1, CTSD, EYS, FTL, GABRG2, GJB2, GJB6, GPR98, GRIN2A, KCNQ2, MECP2, MTRNR1, MYO15A, MYO7A, MYOC, OTOF, PAX2, PCDH15, PCDH19, PDE6A, PDE6B, POLG, PRPF31, PRRT2, RDH12, RP2, RPGR, SCN1A, SCN1B, SCN2A, SCN8A, SLC26A4, SLC2A1, SLC9A6, STXBP1, SYNGAP1, TCF4, TGFBI, TMC1, TMPRSS3, TPP1, TSC1, TSC2, USH1C, USH1G, USH2A, WFS1, ZEB2, HSF4, BFSP2, GALK1, BFSP1, CRYAA, CRYAB, CRYGC, FOXE3, BEST1, NR2E3, NRL, RHO, RP1, RPE65, CAV1, CAV2, SIX1, SIX6, CDKN2B-AS, TMCO1, CYP1B1, LTBP2, PITX2, PAX6, OPN1LW, OPN1MW

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Test Limitations

Some Genes/variations for the following genomic regions may not be reported such as: large genomic rearrangements greater than 50 bp in length, rare (low frequency) mutations, or structural (non-coding) variations and pseudogenes. Rare diagnostics errors may occur if these mutations occur within the priming sequencing regions Presence of a pathogenic/likely pathogenic variant does not guarantee that an individual will develop Hereditary Eye Disease, nor is the absence of such variants a guarantee that an individual will not develop a ' Hereditary Eye Disease '. The results of this genetics screening is strictly meant to guide a physician in the management of their patient's health. Any Likely pathogenic or Pathogenic variants detected in the report should be clinically correlated (As per Physicians Advice) and confirmed via the orthogonal testing platforms (Sanger Sequencing or PCR based tests).

Regulatory Disclosures

Genetic-screening of hereditary Eye Disease predisposition serves as a tool to guide physicians to rule out the clinical condition's genetic origin and helps in the management of their patients and should NOT be treated as a diagnostic tool NGS-based hereditary Eye Disease Risk screening is considered a high-complexity laboratory-developed test (LDT) by CMS under the Clinical Laboratory Improvement Amendment (CLIA) and is not FDA-cleared. The test and performance metrics were validated in house by Elite Clinical Lab technical personnel (or designated scientific advisors) and approved by their Laboratory Director The results are intended for use only by the ordering physician and/or designated healthcare provider. The ordering provider is responsible for 1) ascertaining the medical necessity of the ordered test, 2) resulting diagnoses, 3) management of the disease and/or decisions based on the data provided. Results rely on collection personnel following specified collection and shipment protocols.