

CancerGenomics 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: CGX04172023	Average Read Depth: 211x	



Test Result:

+ Positive : For Likely Pathogenic Variant on MUTYH gene.

Gene & Transcript	Variant	Inheritance	Disorder or Phenotype	Criteria	Classification
MUTYH NM_00112842 5.2	c.1187G>A p.Gly396Asp	Autosomal Recessive / Heterozygous	MUTYH-related attenuated familial adenomatous polyposis	PM1, PP3, PS1	Likely Pathogenic
Location	Allele	State	Allelic Read Depths		
Exon 13	Heterozygous		Ref(C): 405, Alt(T): 361, VAF: 47.13%		
Genomic Position		Variant Frequency			
Chr1:NC_000001.10:g.45797228C>T		0.492% max frequency observed in Annotated gnomAD Non Finnish European			

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Gene info



MUTYH NM_001128425.2

Variant Info



The Variant is found at Chr1:NC_000001.10:g.45797228C>T location with a missense variant c.1187G>A
p.Gly396Asp change on the patient's MUTYH

Variant interpretation



The missense variant NM_001048174.2(MUTYH):c.1103G>A (p.Gly368Asp) causes the same amino acid change as a previously established pathogenic variant. There is a moderate physicochemical difference between glycine and aspartic acid. 2 variants within 6 amino acid positions of the variant p.Gly368Asp have been shown to be pathogenic, while none have been shown to be benign. The p.Gly368Asp missense variant is predicted to be damaging by both SIFT and PolyPhen2. The nucleotide c.1103 in MUTYH is predicted conserved by GERP++ and PhyloP across 100 vertebrates. For these reasons, this variant has been classified as Likely Pathogenic. Overview: An autosomal recessive hereditary neoplastic syndrome caused by mutations in the MUTYH gene on chromosome 1p34.1. It is characterized by the presence of multiple colorectal polyps that may progress to carcinoma. Development of gastric and small intestinal polyps may also occur.

Inheritance



Autosomal Recessive /
Heterozygous

ACMG-Classification

Likely Pathogenic
(PM1, PP3, PS1)

Gene & Disorder or Phenotype

MUTYH-related attenuated familial adenomatous polyposis

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

Cancer Genomics Risk Factor Screening 38 gene panel screening performed at Elite Clinical Laboratory utilizes Next-Generation Sequencing technology using Nextera Flex chemistry on the Illumina MiniSeq and NextSeq platforms. Genomic DNA is extracted from Buccal swabs (Dry and Wet) are tagged 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 Laboratory CGx screen, please contact .

Computational analysis and variant calling is performed by ipseity (www.ipseity.com). Briefly, reads from the sequence 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 Laboratory' analysis work flow 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 endACMG 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 Laboratory's Technical Supervisor or the General Supervisor.

Genes Evaluated

MUTYH, PTEN, BMPR1A, ATM, POLE, CDK4, GJB2, GJB6, BRCA2, BLM, FBN1, GREM1, PALB2, CDH1, RAD51D, COL1A1, BRIP1, TP53, NF1, RAD51C, BRCA1, SMAD4, STK11, POLD1, EPCAM, MSH2, BARD1, MSH6, CHEK2, MLH1, MITF, BAP1, KIT, TERT, APC, PMS2, NBN, CDKN2A

Test Limitations

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 a CGx, nor is the absence of such variants a guarantee that an individual will not develop a 'CGx'. The results of this screen are meant strictly 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).

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Regulatory Disclosures

Genetic-based hereditary CGx Risk Factor screening is intended as a tool to guide physicians in the management of their patients and should NOT be treated as a diagnostic tool. NGS-based hereditary CGx 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 Laboratory 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.

REFERENCES

Richards, Sue, et al. "Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology." *Genetics in medicine* 17.5 (2015): 405. Exome Aggregation Consortium et al. "Analysis of Protein-Coding Genetic Variation in 60,706 Humans." *Nature* 536.7616 (2016): 285–291. PMC. Web. 13 May 2018. The 1000 Genomes Project Consortium. "A Global Reference for Human Genetic Variation." *Nature* 526.7571 (2015): 68–74. PMC. Web. 13 May 2018.

Testing was performed by Elite Clinical Laboratory 3600 S Gessner Road, Houston, TX, 77063 USA CLIA # 45D1061571. Laboratory Director: Dr Albert Chen MD.