ELITE CLINICAL LABORATORY

Cancer Genomics Risk Panel

Patient		Specimen		Ordering Physician	
First Name:	XXXXXXXX	Specimen Type:	Buccal Swab	Physician:	XXXXXXXXX
Last name:	XXXXXXXX	Collection Date:	XX-XX-XXXX	Institution:	XXXXXXXXXXXXX
Date of Birth:	XX-XX-XXXX	Received Date:	XX-XX-XXXX	Reported Date:	XX-XX-XXXX
Gender:	XXXXX	Panel Coverage :	99%	Ref Accession:	N/A
Accession ID:	XXXXXXXX	Average Read Depth:	761x%		

Test Result:

+Positive : For Likely Pathogenic Variant on MUTYH gene.

Gene & Transcript	Variant	Inheritance	Disorder or Phenotype	Criteria	Classification
MUTYH NM_001128425.2	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

Patient

Name : XXXXXXXXX | Date of Birlh: XX-XX-XXXX | Accession : XXXXXXXXXX

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.

Patient

Name : XXXXXXXXX Date of Birlh: XX-XX-XXXX Accession : XXXXXXXXXX

Test Methodology

Cancer Genomics Risk Factor Screening 33 gene panel screening performed at Elite Clinical Laboratory utilizes Next-Generation Sequencing technology using Nextera Flex chemistry on the IIIumina MiniSeq and NextSeq platforms. Genomic DNA is 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 Laboratory CGx screen, please contact .

Computational analysis and variant calling is performed by ipseity (www.ipseitys.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 gnom AD 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 varinats 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

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

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).

Patient

Name : XXXXXXXXX Date of Birlh: XX-XX-XXXX Accession : XXXXXXXXXX

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.