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Lab Director: Neil B Quigley, PhD, HCLD(ABB)
CLIA License ID: 36D2162956

Germline Variant Report

Patient

First name: John
Last name: Doe
Patient ID: library01
DOB: 1 Jan 1970
Gender: Male
Father ethnicity: UNKNOWN
Mother ethnicity: UNKNOWN

Specimen

Accession Number: 20190801003
Specimen Type: Saliva
Collection Date: 08/01/2019
Accession Date: 08/03/2019
Completion Date: 08/03/2019

INTERPRETATION

Positive

This patient is heterozygous for a Pathogenic variant in *BRCA2* gene which has been associated with increased risk of cancer. Consultation with an Oncologist is recommended

RESULTS

SNVs/INDELs (selected in report)

Gene Transcript	Exon	c.DNA Protein alteration	Variant Fraction (ref / alt)	Coding consequence	Pathogenicity	ClinVar
BRCA2 NM_000059.3	11	c.4631delA p.N1544fs*24	32% (68 / 32)	frameshift	Flagged Pathogenicity 5 | Definitely Pathogenic	Pathogenic rs80359460
Comment: The BRCA2 is a tumor suppressor protein involved in DNA repair mechanism. The absence of this protein results in increased DNA damage and increased risk for cancer. The patient has a single nucleotide deleted at position 4631 in *BRCA2* gene. This mutation causes a frame-shift resulting in synthesis of non-functional protein.						
ATM NM_000051.3	31	c.4709T>C p.V1570A	51.46 % (50 / 53)	missense	3 | Variant of Unknown Significance	VUS rs140856217
Comment: The *ATM* gene encodes a serine/threonine kinase that is involved in cell signaling and DNA repair. Certain mutations in *ATM* gene are known to increase cancer risk. The patient has a single nucleotide polymorphism at c.4709T>C. The functional consequence of this variant is unknown.						

Reviewed by:
Date:
Signature:

Approved by: Operator User
Date: 16-03-2018 | 17:34:03
Signature:

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METHODOLOGY AND DISCLAMER

Clariti NGS Methodology

Clariti Diagnostic Laboratories LLC uses Next Generation Sequencing (NGS) technology to analyze coding regions and exon / intron boundaries of selected genes. Nextera Flex For Enrichment chemistry from Illumina is utilized to prepare genomic DNA for sequencing. Genomic DNA is fragmented using Transposomes. Each patient sample is labelled with a unique DNA index to allow libraries to be developed and sequenced simultaneously. Hybrid capture chemistry is utilized to target and then amplify specific regions of interest. The target regions are sequenced with the Illumina Miniseq instrument using either, a mid-output or high-output kit. At least 99.0 % of target regions are covered at 20X or higher.

FASTQ files are analyzed by Sophia Genetics for secondary and tertiary analysis. DNA sequences are assembled and aligned against human genome build GRCh37. The genomic variants are identified and evaluated for clinical relevance using ACMG guidelines. Sanger sequencing is used to confirm Highly Pathogenic variants.

This test was developed and validated by Clariti Diagnostics Laboratories, LLC. Performance parameters were characterized by running extensive set of control samples, patient samples and samples from normal volunteers. The test is not currently FDA cleared. The FDA has determined such clearance for this test is not necessary for laboratories with good standing with CLIA (Clinical Laboratory Improvement Amendments of 1988).

Bioinformatics analysis is provided by Sophia Genetics, Inc (Boston, MA).

Test Limitations and Disclaimer

NGS based sequencing cannot detect genetic mosaicism. Bone marrow transplantation and blood transfusion may affect the test outcome. Some gene regions inherently have low complexity or other properties that make accurate detection of variant difficult. A list of gene regions with low coverage or low sequence complexity in this patient DNA can be obtained by submitting a written request. Clariti Diagnostics Laboratories LLC technology attempts to cover 99.0% of target genes at 20X or higher. PMS2 gene is complicated by the presence of pseudogene. Presence of a pseudogene may affect test results.

Negative result on this test does not rule out the diagnosis of cancer as some genetic mutations may be undetectable with this test. This test is expected to produce highly accurate results. However, the possibility of false negative or false positive due to laboratory errors and data analysis during any step of the testing process cannot be completely ruled out. This test was developed and validated by Clariti Diagnostics Laboratories, LLC. Performance parameters were characterized by running extensive set of control samples, patient samples and samples from normal volunteers. The test is not currently FDA cleared. The FDA has determined such clearance for this test is not necessary for laboratories with good standing with CLIA (Clinical Laboratory Improvement Amendments of 1988).

TEST PERFORMED

Gene Panel (3)

The patient gave his consent to analyse the following genes: *ATM*, *BRCA1*, *BRCA2*