MEDICAL DIAGNOSTIC LABORATORIES L.L.C.

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MDL#: 11721283

Final
Test Results

Physician Copy

Patient Information: **SSN:** **DOB:** 7/1/1993 (Age: 28)

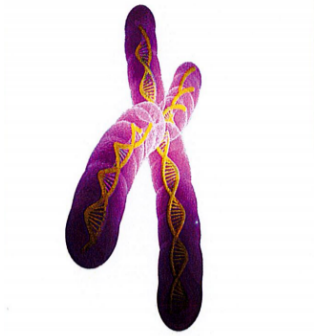
INDIA BATISTE
9126 FORSHEY ST NEW ORLEANS LA 70118

Home: 504-250-9417 **Patient ID:** 7496324

Genetic Counselor Information:

Genetic counseling was waived.

Tel: 504-533-4999
Fax: 504-503-0299



Ordering Physician/Lab: **NPI:** 1801250220

Physician Name: CHARLENE CHAN MD
Physician ID: 63915
1616 CAFFIN STREET NEW ORLEANS LA 70117

Tel: 504-533-4999
Fax: 504-503-0299

Results Faxed To:

Specimen Type:	Saliva
Date Collected:	7/5/2021
Date Processed:	7/7/2021
Date Reported:	7/29/2021

BRCAcare™ 2600: Breast Cancer High Risk Extended Panel Plus

RESULT: Negative for Deleterious Mutation

AFFECTED GENES

ATM (0)	***BARD1*** (0)	***BRCA1*** (0)	***BRCA2*** (0)	***BRIP1*** (0)	***CDH1*** (0)	***CHEK2*** (0)	***NBN*** (0)	***NF1*** (0)	***PALB2*** (0)
PTEN (0)	***RAD51C*** (0)	***RAD51D*** **(1)**	***STK11*** (0)	***TP53*** (0)					

VARIANTS RELEVANT TO INDICATION FOR TESTING

One likely benign variant in RAD51D was identified in this individual. No other variants of relevance to the indication were identified. Please see below for more detailed variant information.

Gene & Transcript	Variant	Allele State	Location	Disorder or Phenotype	Inheritance	Classification
RAD51D NM_002878.3	c.771C>T p.Ser257=	Het.	Exon 9	Unspecified	Autosomal Recessive / Heterozygous	Likely Benign

RECOMMENDATIONS

The interpretation of these results should be done in the context of a patient's medical record and family history. Please note that interpretation and classification of the variants reported here may change over time. Please see a genetic counselor for services regarding the implications of these results in the context of understanding the implications of incidental findings, family planning and the informing of family members of potentially shared genetic outcomes.

APPROACH

Sequencing of the coding regions and flanking non-coding regions of select genes was performed using Next Generation Sequencing and the data was analyzed to identify both previously classified and novel variants in targeted genes. The select gene panel including targeted genes with previous implications of association with breast cancer, ovarian cancer, and/or Lynch syndrome were covered with a minimum read depth of 20X. A multiplex ligation-dependent probe amplification (MLPA) analysis which detects deletions and/or duplications involving one or more exons of ***BRCA1 and BRCA2*** genes was performed. Despite multiple attempts, the submitted sample did not meet MDL's Q/C criteria for reportable results for Deletion/Duplication Analysis assays. If you wish to proceed with this testing, please contact the laboratory directly about submitting an additional DNA sample to perform the test.

DETAILED VARIANT INFORMATION (VARIANTS RELEVANT TO INDICATION FOR TESTING)

Gene & Transcript	Variant	Inheritance	Disorder or Phenotype	Criteria	Classification
RAD51D NM_002878.3	c.771C>T p.Ser257=	Autosomal Recessive / Heterozygous	Unspecified	BS1, BP4, BP7, BP6	Likely Benign

Location	Allele State	Allelic Read Depths
Exon 9	Het.	Ref(G): 226, Alt(A): 211, VAF: 48.28%

Genomic Position	Variant Frequency
NC_000017.10:g.33428352G>A	0.652% max frequency observed in gnomAD Exomes Annotation

VARIANT INTERPRETATION: The synonymous variant NM_002878.4(RAD51D):c.771C>T (p.Ser257=) has been reported to ClinVar as Benign/Likely Benign with a status of (2 stars) criteria provided, multiple submitters, no conflicts (Variation ID 138875 as of 2021-07-01). The p.Ser257= variant is observed in 106/16,254 (0.6521%) alleles from individuals of gnomAD African background in gnomAD, which is greater than expected for the disorder. The p.Ser257= variant is not predicted to disrupt an existing splice site. The p.Ser257= variant results in a substitution of a base that is not predicted conserved by GERP++ and PhyloP. For these reasons, this variant has been classified as Likely Benign.

METHODOLOGY

The individual's DNA was extracted and fragmented, with fragments from the coding regions and flanking non-coding regions of the select gene panel targeted for amplification and sequencing. Reads from the sequence output were aligned to the human reference genome (GRCh37) and variants to the reference were called using Sentieon DNAseq (vs. 2018.08.07). The variants were annotated and filtered using the Golden Helix VarSeq (vs 2.2.0) analysis workflow implementing the ACMG guidelines for interpretation of sequence variants. This includes comparisons 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 variant results are reported using numbering and nomenclature recommended by the Human Genome Variation Society (HGVS http://hgvs.org). Nucleotide and codon number are based on the gene transcript: ***ATM*** (NM_000051.3), ***BARD1*** (NM_000465.3), ***BRCA1*** (NM_007294.3), ***BRCA2*** (NM_000059.3), ***BRIP1*** (NM_032043.2), ***CDH1*** (NM_004360.3), ***CHEK2*** (NM_007194.3), ***NBN*** (NM_002485.4), ***NF1*** (NM_000267.3), ***PALB2*** (NM_024675.3), ***PTEN*** (NM_000314.6), ***RAD51C*** (NM_058216.2), ***RAD51D*** (NM_002878.3), ***STK11*** (NM_000455.4) and ***TP53*** (NM_000546.5).

In addition to the gene sequencing assay, a MLPA analysis which detects deletions and/or duplications involving one or more exon, including those that affect the entire ***BRCA1 and BRCA2 genes,*** was completed.

VARIANT ASSESSMENT PROCESS

The following databases and ***in silico*** 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 RefSeq Genes, ExAC Gene Constraints, VS-SIFT, VS-PolyPhen2, PhyloP, GERP++, GeneSplicer, MaxEntScan, NNSplice and PWM Splice Predictor. Analysis was reported using the HGVS nomenclature (www.hgvs.org/mutnomen) as implemented by the VarSeq transcript annotation algorithm. The reported transcript matches that used most frequently by clinical laboratories submitting to ClinVar.

LIMITATIONS

It should be noted that this test is performed on a limited number of genes and does not include all intronic and non-coding regions. This assay cannot detect mutations affecting gene regions not examined in the assay. Intronic regions are analyzed up to 10 nucelotides before and 10 nucleotides after each intron/extron boundary. This report only includes variants that meet a level of evidence threshold for cause or contribution to disease. Certain classes of genomic variants are also not covered using the NGS testing technology, including triplet repeat expansions, copy number alterations, translocations and gene fusions or other complex structural rearrangements. More evidence for disease association of genes and causal pathogenic variants are discovered every year, and it is recommended that genetic variants are re-interpreted with updated software and annotations periodically.
This test was developed and its performance characteristics have been determined by Medical Diagnostic Laboratories, LLC. Performance characteristics refer to the analytical performance of the test. It is not been reviewed by the US Food and Drug Administration (FDA). The FDA has determined that such clearance or approval is not necessary.

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.

DRAFT REPORT