PrimaHealth

CGX Advantage Cancer Genomics Test Report

PATIENT INFORMATION

Name:	DOE, JANE	**Accession Number:**	1245628479
Date of Birth:	04/18/1956	**Client:**	
Gender:	Female	**Ordering Physician:**	JOHN SMITH MD
Date Received:	04/14/2016	**Date Accessioned:**	04/14/2016
Date Collected:	04/14/2016	**Date Reported:**	04/19/2016
		Review Status	Final

TEST PERFORMED

BreastDetect Targeted next-generation sequencing was performed on this specimen. See under Test Details for more information.

RESULT SUMMARY

Variants Detected	Classification
BRCA1 p.E143*	Pathogenic
TP53 p.P33R p.P72R	Variant of Uncertain Significance
NBN p.E103Q p.E185Q	Variant of Uncertain Significance

CLINICALLY RELEVANT RESULTS

BRCA1
p.E143*
Pathogenic

Interpretation: A nonsense mutation in BRCA1, p.E143*, was detected in a heterozygous state. This mutation is predicted to result in a non-functional BRCA1 protein product due to the introduction of a premature termination codon. This specific mutation has been previously reported in the medical literature and clinical databases and is considered pathogenic in nature. The BRCA1 p.E143* alteration is reported as a founder mutation within the Irish population and has also been documented in individuals of European descent (Janaviius R;Founder BRCA1/2 mutations in the Europe: implications for hereditary breast-ovarian cancer prevention and control.; EPMA J; 2010 Sep;1(3):397-412);(McVeigh TP, et al.; Familial breast cancer genetic testing in the West of Ireland.; Ir J Med Sci; 2014 Jun;183(2):199-206). Germline BRCA1 alterations are associated with Hereditary Breast and Ovarian Cancer syndrome, an autosomaldominant condition in which mutation carriers are at increased risk to develop cancers of the breast, ovary, pancreas and prostate,among others. (Foulkes WD; BRCA1 and BRCA2 - update and implications on the genetics of breast cancer: a clinicalperspective.; Clin Genet; 2014 Jan;85(1):1-4).

TEST DETAILS

BreastDetect: Targeted next-generation sequencing was performed on this specimen.

BreastDetect: *ATM*, *BRCA1*, *BRCA2*, *BRIP1*, *CDH1*, *CHEK2*, *MUTYH*, *NBN*, *NF1*, *PALB2*, *PTEN*, *RAD51C*, *RAD51D* and *TP53* were subjected to targeted next generation sequencing analysis.

Database Details: The version/release/build/date of the following databases were used to generate this report.

- Genomic Build: GRCh37.p13
- Genomic Anotation Sources: NCBI RefSeq v105
- ExAC: v0.3
- dbSNP: 141
- ClinVar: 20150603
- NHLBI ESP: v.0.0.30
- dbNSFP: 3.0b2c

Coding Exon Coverage Metrics: 10x coverage for >90% of positions was not achieved for some targeted exons. If interested in viewing these regions, please consult with a certified genetic counselor.

METHODOLOGY

Experimental Methodology: This test uses targeted next-generation sequencing (NGS) to analyze coding regions of the most inclusive annotated RefSeq transcript for each of the targeted genes. Target exome enrichment was performed using probe based targeted capture using Agilent HaloPlex HS Custom Panel. Sequencing of enriched libraries was performed in multiplex on the Illumina MiSeq.

Informatics Methodology: There are four informatics tools used and relevant parameters used for each tool are detailed as follows:

1. Trim Galore
Version 0.4.0 (uses Cutadapt Version 1.8)
Parameters: --path_to_cutadapt (path to Cutadapt) -a AGATCGGAAGAGCACACGTCTGAACTCCAGTCAC -a2 AGATCGGAAGAGCGTCGTGTAGGGAAAGAGTGTAGATCTCGGTGGTCGCCGTATCATT --paired --clip_R1 5 --clip_R2 5 --three_prime_clip_R1 5 --three_prime_clip_R2 5
2. Novoalign
Version 3.02.07
Parameters: -o SAM -r none --softclip 9999 -l 30 -e 100 -i 230 140 -t 300 -H
3. samtools
Version 0.1.19
Parameters: -B -d 1000000'
4. Freebayes Version v0.9.21-19-gc003c1e
Parameters: --use-duplicate-reads --min-alternate-count 10 --min-alternate-fraction 0.20 --min-coverage 10 --min-base-quality 20 --min-mapping-quality 30 --min-supporting-allele-qsum 20 --min-supporting-mapping-qsum 30 --min-alternate-qsum 40 --use-mapping-quality

Novoalign is an alignment tool. Freebayes is a variant caller used to identify substitutions, insertions, and deletions.

Note that it is possible that pathogenic variants may not be reported by one or more of the tools because of the parameters used. However, tool parameters were optimized to maximize specificity and sensitivity.

DISCLAIMER

This Report was generated using the materials and methods described above. Such materials and methods required the use of various reagents, protocols, instruments, software, databases, and other items, some of which were provided or made accessible to Laboratory Name ("LAB") by third parties. A defect or malfunction in any such reagents, protocols, instruments, software, databases, and/or other items may compromise the quality or accuracy of the Report.

The Report is based on, or incorporates by mention thereto, various scientific manuscripts, references, and other sources of information. Such may include without limitation manuscripts, references, and other sources of information that were prepared by third parties describing correlations between certain genetic mutations and particular diseases (and/or certain therapeutics that may be useful in ameliorating the effects of such diseases). Such information and correlations are subject to change over time in response to future scientific and medical findings. LAB makes no representation or warranty of any kind, expressed or implied, regarding the accuracy of the information contained in such manuscripts, references, and other sources of information. If any of the information provided by or contained in such manuscripts, references, and other sources is later determined to be inaccurate, the accuracy and quality of the Report may be adversely impacted. LAB is not obligated to notify you of any impact that future scientific or medical research findings may have on the Report.

The Report must always be interpreted and considered within the clinical context, and a physician should always consider the Report along with all other pertinent information and data that a physician would prudently consider prior to providing a diagnosis to a patient or developing and implementing a plan of care for a patient. The Report should never be considered or relied upon alone in making any diagnosis or prognosis. The manifestation of many diseases are caused by more than one gene variant, a single gene variant may be relevant to more than one disease, and certain relevant gene variants may not have been considered in the Report. In addition, many diseases are caused or influenced by modifier genes, epigenetic factors, environmental factors, and other variables that are not addressed by the Report (or that are otherwise unknown). As such, the relevance of the Report should be interpreted in the context of a patient's clinical manifestations. The Report provided by LAB is provided on an "AS IS" basis. LAB makes no representation or warranty of any kind, expressed or implied, regarding the Report. In no event shall LAB be liable for any actual damages, indirect damages, and/or special or consequential damages arising out of or in any way connected with the Report, your use of the Report, your reliance on the Report, or any defect or inaccurate information included within the Report.

Medical knowledge annotation is constantly updated and reflects the current knowledge at the time.

The test performance characteristics were determined by the Pierian DX. The Report was generated by Pierian DX as required by the CLIA 1988 regulations. The Report, and the tests used to generate the Report, have not been cleared or approved by the U.S. Food and Drug Administration (FDA). The FDA has determined that such clearance or approval is not necessary. The test results have been shown to be clinically useful. This laboratory is CLIA certified to perform high complexity testing.

Approved and verified by LAB certified genetic counselors. Questions regarding results should be sent to GeneticCounselors@LAB.com or can be addressed at (678) 123-4567.

Report Electronically reviewed and signed out by:

Date Reported: 04/19/2016