Patient Information

Name:	VANAJA M
Age/Gender:	60 years/ Female
Referring Physician:	Dr. Gopi K R
Referring Centre:	Dr. Gopi K R - Cochin
Specimen Type:	Peripheral Blood
Sample ID:	2400020095
Patient ID:	10023134285
Date received:	31.01.2024
Report Date:	16.02.2024

BRCA1 & *BRCA2* GERMLINE MUTATION TESTING

Clinical History

Ms. VANAJA M, is a case of Ca Breast with lung metastasis. She has been evaluated for pathogenic variations in the BRCA1 and BRCA2 genes..

Result

No clinically relevant pathogenic or likely pathogenic mutations was detected in *BRCA1* and *BRCA2* genes.

Recommendation

• Breast cancers are also associated with germline mutations in a variety of other genes, patient is advised to undergo multigene panel testing which covers high risk Ovarian Cancer genes (ATM, BRIP1, NBN, PALB2, STK11, RAD51C, RAD51D MLH1, MSH2, MSH6, PMS2).
• Genetic Counselling consultation is recommended to understand genetic testing options for cancer risk, including benefits, risks, and limitations.

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GM-Genomics Operations

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Supplementary Information

Methodology

DNA was extracted from the given specimen by using QIAMP blood nucleic acid extraction kit. The library was prepared using Oncomine *BRCA* Research Assay primer pools and Ion Ampliseq ™ Library Kit. The libraries prepared from individual samples were barcoded using Ion Xpress™ barcodes. These libraries were then sequenced on S5 Ion torrent instrument. The data was analyzed using Ion torrent software Oncomine reporter software. The lower limit of detection for variant allelic frequency (VAF) as per the manufacturer's instructions is 5%

Quality control Statistics

Coverage within target regions	100%

Genes Analyzed

All exonic regions and exon intron boundaries of *BRCA1* & *BRCA2* genes.

Variant Classification

Genetic test results are reported based on the recommendations of the American College of Medical Genetics (ACMG) as described below [PMID: 25741868] :

Variant	A change in a gene. This could be disease causing (pathogenic) or not disease causing (benign).
Pathogenic	A disease causing variation in a gene which can explain the patient's symptoms has been detected. This usually means that a suspected disorder for which testing had been requested has been confirmed.
Likely Pathogenic	A variant which is very likely to contribute to the development of disease. However, the scientific evidence is currently insufficient to prove this conclusively. Additional evidence is expected to confirm this assertion of pathogenicity.
Variant of Uncertain significance	A variant is difficult to classify it as either pathogenic (disease causing) or benign (non-disease causing) based on current available scientific evidence. Further testing of the patient or family members as recommended by your clinician may be needed. It is probable that their significance can be assessed only with time, subject to availability of scientific evidence.

References

1- 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 : official journal of the American College of Medical Genetics vol. 17,5 (2015): 405-24. doi:10.1038/gim.2015.30

2- Golan, Talia et al. "Maintenance Olaparib for Germline BRCA-Mutated Metastatic Pancreatic Cancer." The New England journal of medicine vol. 381,4 (2019): 317-327. doi:10.1056/NEJMoa1903387

3- Litton, Jennifer K et al. "Talazoparib in Patients with Advanced Breast Cancer and a Germline BRCA Mutation." The New England journal of medicine vol. 379,8 (2018): 753-763. doi:10.1056/NEJMoa1802905

4- O'Shaughnessy, Joyce et al. "Prevalence of germline BRCA mutations in HER2-negative metastatic breast cancer: global results from the real-world, observational BREAKOUT study." Breast cancer research : BCR vol. 22,1 114. 27 Oct. 2020, doi:10.1186/s13058-020-01349-9
5- Litton, Jennifer K et al. "Neoadjuvant Talazoparib for Patients With Operable Breast Cancer With a Germline BRCA Pathogenic Variant." Journal of clinical oncology : official journal of the American Society of Clinical Oncology vol. 38,5 (2020): 388-394. doi:10.1200/JCO.19.01304
6- Malhotra, Hemant et al. "Genetic Counseling, Testing, and Management of HBOC in India: An Expert Consensus Document
7- https://cancer.sanger.ac.uk/cosmic
8- https://www.mutationtaster.org/
9- http://www.ncbi.nlm.nih.gov/snp
10- http://browser.1000genomes.org
11- http://www.mycancergenome.or
12- http://genetics.bwh.harvard.edu/pph2
13- http://sift.jcvi.org
14- http://mutationassessor.org

Disclaimer

- This report is based on the sample received in the Lilac Insights laboratory; the analysis is based on the assumption that samples received are representative of the patient name mentioned on the test requisition form and the sample tube. When samples are received from various referral centers, it is presumed that patient demographics are verified at the point of sample collection.
- The *BRCA1* and *BRCA2* germline testing is validated in-house as per the standard Next Generation Sequencing validation protocols.
- Despite all the necessary precautions and stringency adopted whilst performing DNA tests, the currently available data indicates that the technical error rate associated with all types of DNA analysis, is approximately 2%. Although molecular testing is highly accurate, rarely false-positive & false-negative diagnostic errors may occur due to improper quality control during sample collection, cellular integrity of sample, selection of inappropriate specimen and/or presence of PCR inhibitors. PCR primer binding site polymorphisms or mutations might lead to allele dropout & cause false negative results. It is important that all clinicians or persons requesting DNA diagnostic tests are aware of these data before acting upon these results.
- As with all diagnostic tests, the laboratory report must be interpreted in conjunction with the presenting clinical profile of the patient and evaluation of all reports. In sequencing based tests sometimes variants of unknown significance (VUCS) are detected that have either not been reported before, and/or whose effect cannot be determined based on the current knowledge standards and reporting guidelines. In such cases, we recommend periodic review of these variants to determine any change in classification based on new published research.
- The mutations have not been validated/ confirmed by Sanger sequencing. Sanger confirmation of reported mutations is available on request with additional charges.
- The classification and interpretation of all the variants is carried out based on the current state of scientific knowledge and medical understanding and may change over time with more information available in future.
- This report should not be considered as medical advice. Results of this test need be interpreted within the context of clinical findings and other relevant clinical and laboratory data and should not be used alone.
- Likely benign and benign variants are not reported.

End Of Report

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