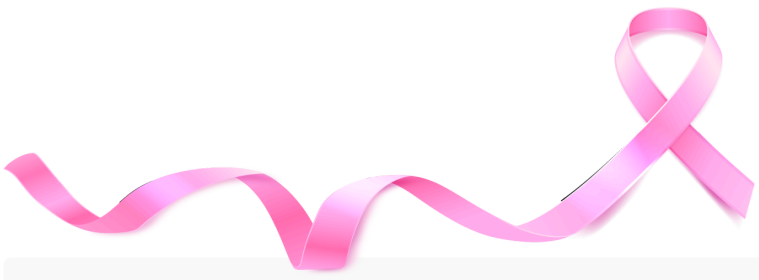
LABORATORY REPORT

Redcliffe labs



BRCA Report

Patient Name	:	**Booking ID:**	:
Age:	:	**Sample Type:**	:
Gender	:	**Sample Collection Date:**	:
Referring Clinician	:	**Sample Collection Time:**	:
Barcode No:	:	**Reporting Date:**	:

Test Performed:-BRCA1 & BRCA2 Mutation Analysis Test By NGS

Clinical Indication:

ain over the left upper limb and left breast. PET scan reveals an FDG-avid, heterogeneously dense soft tissue mass involving the entire right breast

TEST RESULTS

Negative

No clinically relevant variant detected in BRCA1 & 2 gene related to clinical phenotype

Key Finding

Gene & Transcript	Exon	Variant	Zygosity	Inheritance	ACMG Classification
NA	NA	NA	NA	NA	NA

Detailed Variant Information (Variants Relevant To Indication For Testing)

No pathogenic, no likely pathogenic, no variant of uncertain significant variant in BRCA1& 2 genes were detected related to clinical phenotype in the given blood sample. We do not report benign/likely benign variant ndings as per ACMG guidelines for the reporting criteria. We can share the bening/likely benign based variant upon clinician's request if any

Note: This is a sample report for illustrative purpose only. Actual report may vary

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QC Metrics

Number of mapped reads	1,472,757
Percent reads on target	99.16%
Average base coverage depth	6,400
Uniformity of base coverage	97.94%
Target base coverage at 20x	100.00%
Target base coverage at 100x	100.00%

Recommendations:

Based on the clinical features and the observed genetic findings the following have been recommended:

1. Please correlate clinically.
2. Genetic counselling is recommended for the patient to discuss the potential clinical implications of this result.
3. MLPA analysis of BRCA1 & 2 genes is suggested to rule out the presence of any large deletion/duplication or copy- number variations (CNVs).
4. If above results do not correlate completely with phenotype or family history, additional testing HBOC or BRCA expanded/HRR NGS panel test is advised based on doctor's recommendation.

Test Description:

BRCA1 (BReast CAncer gene 1) and BRCA2 (BReast CAncer gene 2) are genes that produce proteins that help repair damaged DNA. Everyone has two copies of each of these genes--one copy inherited from each parent. BRCA1 and BRCA2are tumor suppressor genes. When they have certain changes, called pathogenic variants (or mutations), cancer can develop..

People who inherit pathogenic variants in one of these genes have increased risks of several cancers-most notably breast and ovarian cancer, but also several additional types of cancer. People who have inherited a pathogenic variant in BRCA1 and BRCA2 also tend to develop cancer at younger ages than people who do not have such a variant.

This test uses Next Generation Sequencing, targeted sequencing approach that is restricted to the protein-coding regions of selected genes under investigation. BRCA1 and BRCA2 Panel contains primer pairs that target the coding regions of the tumor suppressor genes BRCA1 and BRCA2, which have been implicated in hereditary breast and ovarian cancers.

What is a positive BRCA result?

A positive test result means that a genetic change (variant) was found in the BRCA gene. A positive BRCA variant is considered "pathogenic" or "likely pathogenic" because it is associated with hereditary breast and ovarian cancer (HBOC) syndrome.

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What does this mean?

It is possible for anyone to get cancer at some point in their life, however, individuals with HBOC are more likely to get certain cancers compared to the average person. There is an increased chance for female breast cancer (53-78% and a 20-42% chance of developing a second breast cancer within 10 years), male breast cancer (1-2%), ovarian cancer (44-65%), pancreatic cancer (3-4%), and prostate cancer (7-26%). There may also be an increased chance for melanoma, however, lifetime risks are not clear. Some people inherit two BRCA variants, which may cause a rare condition called Fanconi anemia. See the table later in this guide for ways to manage HBOC.

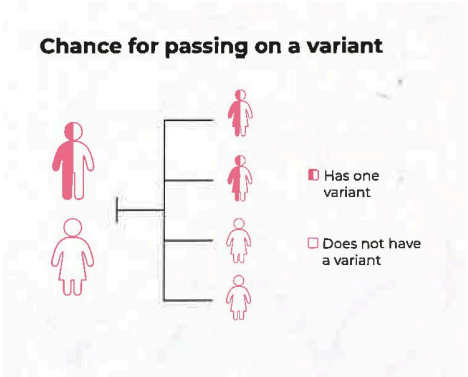
What does this mean for family members?

The image on the right demonstrates how variants in BRCA can be passed on from generation to generation.

Who should be tested next?

Parents, siblings, children, and other relatives may also have this BRCA variant. Both men and women can inherit and pass on a BRCA variant. People may have different conditions or symptoms depending on whether they inherit one or two variants in BRCA. For individuals who are planning a family, reproductive options may be available to help lower the chance of passing on the variant to a child.

A BRCA variant affects everyone differently. Family members with the variant may develop cancer at different ages, or they may never develop cancer.



Methodology

BRCA1 & BRCA2 Panel on Next Generation Sequencing is a targeted sequencing approach that is restricted to the protein-coding regions of selected genes under investigation. BRCA1 and BRCA2 Panel contains primer pairs pool that target the coding regions of the tumor suppressor genes BRCA1 and BRCA2, which have been implicated in breast and ovarian cancers. This targeted NGS panel utilizes 265 amplicons to analyze the coding region of both BRCA1 and BRCA2 genes including intron-exon boundary of 10 bases from both upstream & downstream region. DNA isolated from Peripheral Blood is used for NGS Library preparation. The libraries were sequenced to mean depth: >150x on the next generation sequencing platform. The read sequences obtained in the format of a BAM file from Ion torrent sequencer are processed to filter out poor quality reads using standard bioinformatics tools & software. Clinically relevant germline variants were analysed and annotated using published variants in literature and a set of diseases databases. Clinically relevant germline variants were annotated using published variants in literature and a set of diseases databases ClinVar, ClinVar miner, gnomAD, UCSC, OMIM, & HGMD. The effect of non-synonymous variants is calculated using multiple prediction algorithms such as PolyPhen, SIFT, Mutation Taster2.

Test Limitations

- It should be noted that this test is limited to only BRCA1 and BRCA2 genes and does not include all intronic and non-coding regions.
- This report only includes variants that meets a level of evidence threshold for cause or contribute to disease.
- Certain classes of genomic variants are also not covered in this test, 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.

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Variant Classification Based On Acmg Recommendations

Genetic test results are reported based on the recommendations of American College of Medical Genetics (ACMG) as described below [1].

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 patients' symptoms.
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 which is difficult to classify either as pathogenic (disease causing) or benign (non-disease causing) based on current available scientific evidence.

Disclaimer

- Interpretation of variants in this report is performed to the best knowledge of the laboratory based on the information available at the time of reporting. The classification of variants can change over time and laboratory cannot be held responsible for this. Re-analysis of variants in previously issued reports in light of new evidence is not routinely performed, but may be available upon request.
- Negative results do not completely exclude the risk/carrier status for these disorders tested (residual risk)
- The test methodology currently does not detect large deletions/duplications, deep intronic variants, and regulatory region variants.
- Phenotype variability may be due to modifying genetic/non-genetic factors and is not a part of the current analysis.
- Variants of unknown significance may be detected and may not be reported subject to analysis by various methodologies.
- Due to inherent technology limitations of the assay, not all bases of the genes can be covered by this test. Accordingly, variants in regions of insufficient coverage may not be identified and/or interpreted. Therefore, it is possible that pathogenic variants are present in one or more of the genes analyzed, but have not been detected. The variants not detected by the assay that was performed may impact the phenotype.
- It is also possible that a pathogenic variant is present in a gene that was not selected for analysis and/or interpretation in cases where insufficient phenotypic information is available.
- Genes with pseudogenes, paralog genes and genes with low complexity may have decreased sensitivity and specificity of variant detection and interpretation due to inability of the data and analysis tools to unambiguously determine the origin of the sequence data in such regions.
- If variants are detected, Sanger sequencing confirmation is needed.
- Incidental or secondary findings (if any) that meet the ACMG guidelines can be given upon request.
- The report shall be generated within turnaround time (TAT), however, such TAT may vary depending upon the complexity of test(s) requested. Laboratory under no circumstances will be liable for any delay beyond aforementioned TAT.
- It is hereby clarified that the report(s) generated from the test(s) do not provide any diagnosis or opinion or recommends any cure in any manner. Laboratory hereby recommends the patient and/or the guardians of the patients, as the case may be, to take assistance of the clinician or a certified physician or doctor, to interpret the report(s) thus generated. Laboratory hereby disclaims all liability arising in connection with the report(s).
- In a very few cases genetic test may not show the correct results, e.g. because of the quality of the material provided to laboratory. In case where any test provided by laboratory fails for unforeseeable or unknown reasons that cannot be influenced by laboratory in advance, laboratory shall not be responsible for the incomplete, potentially misleading or even wrong result of any testing if such could not be recognized by laboratory in advance.

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References

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Conditions for Reporting

1. It is presumed that specimen belongs to patient named or identified, such verification being carried out at the point of generation of said specimen.
2. A test might not be performed due to following reasons:
    a. Specimen Quantity not sufficient (Inadequate collection/spillage during transit).
    b. Specimen Quality not acceptable (Hemolysis/clotted/lipemic).
    c. Incorrect sample type.
3. In any of the above case a fresh specimen will be required for testing and reporting.
4. Partial representation of report is not allowed.
5. The reported tests are for the notification of the referring doctor, only to assist him/her in the diagnosis and management of the patient.
6. This report is not valid for Medico Legal Purpose.
7. Applicable Jurisdiction will be of "Delhi" for any dispute/claim concerning the test(s) & results of the test(s).

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Terms and Conditions of Reporting

1. The presented findings in the Reports are intended solely for informational and interpretational purposes by the referring physician or other qualified medical professionals possessing a comprehensive understanding of reporting units, reference ranges, and technological limitations. The laboratory shall not be held liable for any interpretation or misinterpretation of the results, nor for any consequential or incidental damages arising from such interpretation.

2. It is to be presumed that the tests performed pertain to the specimen/sample attributed to the Customer's name or identification. It is presumed that the verification particulars have been cleared out by the customer or his/her representation at the point of generation of said specimen / sample. It is hereby clarified that the reports furnished are restricted solely to the given specimen only.

3. It is to be noted that variations in results may occur between different laboratories and over time, even for the same parameter for the same Customer. The assays are performed and conducted in accordance with standard procedures, and the reported outcomes are contingent on the specific individual assay methods and equipment(s) used, as well as the quality of the received specimen.

4. This report shall not be deemed valid or admissible for any medico-legal purposes.

5. The Customers assume full responsibility for apprising the Company of any factors that may impact the test finding. These factors, among others, includes dietary intake, alcohol, or medication / drug(s) consumption, or fasting. This list of factors is only representative and not exhaustive.