Booked For
Dr Nagendra Parvataneni, Kims Hospital,Secunderabad , - 500003
Contact No. -9703440407

Processed By
Gurugram, Plot No. 55-56, Udhyog Vihar Ph-IV, - 122015
Contact No. -7500075111

Name	**: Mrs. KARUNA P A**	Billing Date	: 16/07/2025 01:49:44 PM
Age/Gender	: 41 Yrs/Female	Sample Collected on	: 16/07/2025 01:49:59 PM
P. ID No.	: 32002507167948F760	Sample Received on	: 17/07/2025 07:34:28 AM
Accession No	**: 3200L20257160011**	Report Released on	: 29/07/2025 01:12:40 PM
Referring Doctor	: DR NAGENDRA PARVATHANENI		
Referred By	:		

Report Status -Final

BRCA 1 & 2 Germline Test

Refer Attachment

** End of Report **

Authenticated By

Dr. Sarjana Dutt
PhD, PDF
Lab Director- NRL

3200L20257160011

Please scan the QR code to check authenticity of report

Patient Name: KARUNA P A
VID: 3200L20257160011

CLINICAL DIAGNOSIS/ HISTORY/ INDICATION FOR TESTING

C/O Invasive Ductal Carcinoma (R) Breast; HR +ve, HER2 -ve. The Test is being performed on Whole Blood EDTA Sample for Risk Prediction/ Prognosis/ Theranostics

RESULT & INTERPRETATION

PATHOGENIC VARIANT DETECTED IN BRCA1 GENE

NO PATHOGENIC/ LIKELY PATHOGENIC/ VUS WAS DETECTED IN BRCA2 GENE

Gene (Transcript #)	Location	Variant Detected	Zygosity	Disease (OMIM)	Inheritance	Classification
BRCA1 NM_007294.4	Exon 23	c.5503C>T/ p.Arg1835Ter	Heterozygous	Hereditary Breast Ovarian Cancer Syndrome	Autosomal Dominant	Pathogenic

Result: c.5503C>T/ p.Arg1835Ter was detected in the BRCA1 gene of the sample tested. **ClinVar** describes this mutation as **Pathogenic**.

Significance:
The p.R1835* pathogenic mutation (also known as c.5503C>T), located in coding exon 23 of the BRCA1 gene, results from a C to T substitution at nucleotide position 5503. This changes the amino acid from an arginine to a stop codon within the coding exon. Premature stop codons are typically deleterious in nature and the impacted region is critical for protein function. This mutation has been detected in multiple hereditary breast and ovarian cancer (HBOC) syndrome cohorts to date (Serova O et al. Am. J. Hum. Genet. 1996 Jan;58:42-51; Rashid MU et al. BMC Cancer. 2016 08;16:673; Meisel C et al. Arch. Gynecol. Obstet. 2017 May;295:1227-1238; Sun J et al. Clin. Cancer Res. 2017 Oct;23:6113-6119; Heramb C et al. Hered. Cancer Clin. Pract. 2018 Jan;16:3; Apessos A et al. Cancer Genet. 2018 01;220:1-12). One functional study found that this nucleotide substitution is non-functional in a high-throughput, genome editing, haploid cell survival assay (Findlay GM et al. Nature, 2018 10;562:217-222). Of note, this alteration is also designated as 5622C>T in published literature. Based on the supporting evidence, this alteration is interpreted as a disease-causing mutation; hence, this variant is classified as Pathogenic.

Recommendations:
1) The patient may be evaluated for treatment with PARPi, if indicated as per clinical history
2) Suitable members of the family may be counselled for Genetic Testing for Cancer predisposition
3) The patient may be evaluated for Risk reduction strategies if Test has been performed for Screening

Classification of Variant	Remarks
Pathogenic	This variant has been shown to directly contribute to the development of disease. The subject is at significantly increased risk for developing Breast and / or Ovarian cancer as compared to the general population

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Likely Pathogenic	There is a high likelihood (> 90% certainty) that this variant is disease-causing. Additional evidence is expected to confirm this assertion of pathogenicity; however, there is also a small chance that new evidence may demonstrate that this variant is non-pathogenic.
Likely Benign	This variant is not expected to have a major effect on disease; however, the scientific evidence is currently insufficient to prove this conclusively. Additional evidence is expected to confirm this assertion, but one cannot fully rule out the possibility that new evidence may demonstrate a disease causing association
Benign	This variant does not contribute to causing the disease.
Variant of Unknown Significance (VUS)	There is not enough information at this time to support a more definitive classification of this variant.

COMMENTS & RECOMMENDATIONS

1. Large deletions/ duplications or complex rearrangements are not covered in the given test. The same may be investigated through MLPA testing.
2. A positive test result cannot tell whether or when an individual will develop cancer. Also, a positive test result may have important implications for family members, including future generations. The first degree relative has a 50% chance of inheriting the mutation.
3. The lifetime risk of Breast cancer with the pathogenic variant of BRCA1 and BRCA 2 is 46% to 87%. Also, BRCA germline pathogenic variants confer an excessive risk for ovarian cancer ranging from 16.5% to 63%.
4. The lifetime risk of prostate cancer with germline pathogenic variants in BRCA genes ranges from 20-30%.
5. Genetic Counselling is recommended to discuss the implications of this test result for the individual. This counselling should be performed by a health care professional who is experienced in cancer genetics.

CLINICAL INFORMATION

1. Many people have a family history of cancer, however, only 5-10% of cancer is hereditary. Individuals who are born with deleterious mutations in certain key genes are at an elevated lifetime risk of developing cancer
2. Specific inherited mutations in BRCA1 and BRCA2 genes increases the risk of HBOC. Hereditary cancer genetic testing should be considered in the following scenarios-
    a. If the subject or family members (first- and second-degree blood relatives) have been diagnosed with early onset breast cancer (age <45yrs) or triple negative (ER-/PR-/HER2-) breast cancer at an age <60 yrs
    b. If the subject or family members have been diagnosed with more than one cancer, such as bilateral breast cancers, or breast and ovarian cancer
    c. A personal history of ovarian cancer or male breast cancer
    d. A personal history of breast cancer and one or more relatives with breast cancer diagnosed before age 50, two or more relatives diagnosed with breast cancer at any age, one or more relatives with ovarian cancer, one or more relatives with male breast cancer, or two or more relatives with prostate cancer or pancreatic cancer
    e. A personal history of breast cancer and Ashkenazi (Eastern European) Jewish ancestry
    f. A personal history of prostate cancer or pancreatic cancer with two or more relatives with BRCA-associated cancers
    g. A history of breast cancer at a young age in two or more first degree blood relatives

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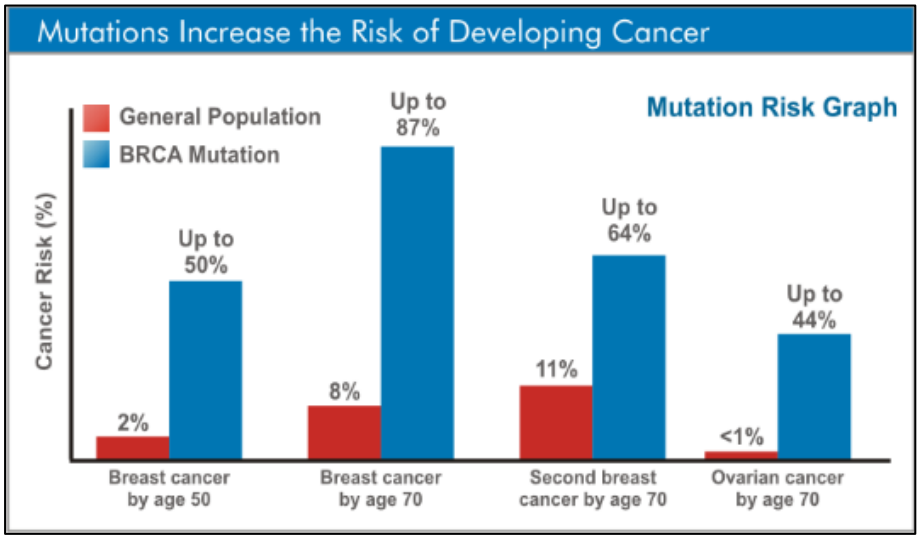
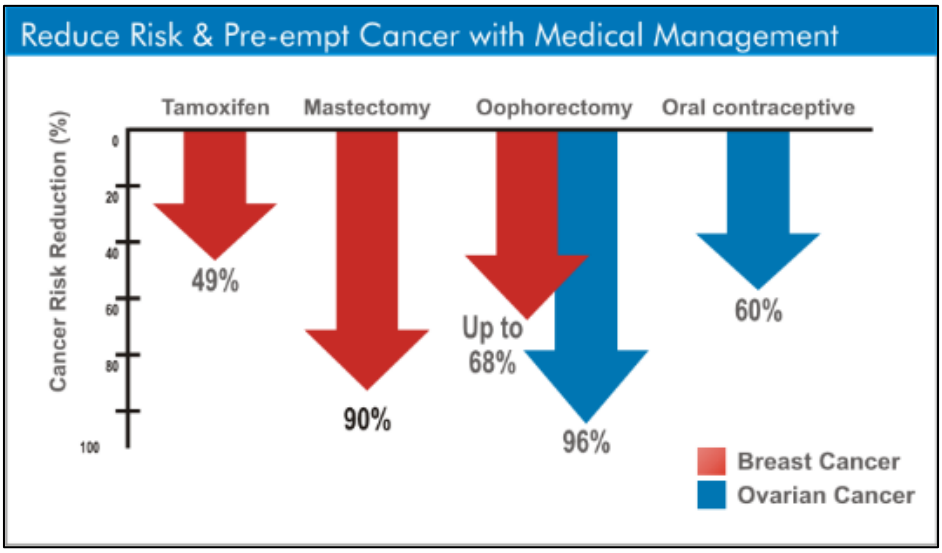
h. A relative with a known BRCA1 or BRCA2 mutation



3. If a deleterious mutation is identified, then various options may be considered for reduction of risk, such as use of Tamoxifen, bilateral mastectomy, Oophorectomy or Oral contraceptives.



TEST INFORMATION

This test analyzes genetic variants in BRCA1 & BRCA2 genes associated with hereditary Breast and Ovarian cancer predisposition as per NCCN & ACMG guidelines. Large deletions/ duplications or complex rearrangements are not covered in the given test. The same may be investigated through MLPA testing.

Patient Name: KARUNA P A
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This test involves preparation of a target sequence amplification and enrichment-based library from the patient's Genomic DNA using Ampliseq Technology. The test has a variation coverage for all coding regions (100% for BRCA1 and 99.70% for BRCA2).

METHODOLOGY & TEST ATTRIBUTES

DNA Extraction: Genomic DNA was isolated by using commercial validated kit and was quantified by Qubit Fluorometer (ThermoFisher).
Library Construction: The library construction was done using Ampliseq technology. Fragmentation was done further to prepare the DNA sequencing library using enzyme digestion. The resulting DNA fragments were then ligated to technology-specific adaptor sequences. These adaptors have a unique molecular "barcode", so each sample can be tagged with a unique DNA sequence. This allows for multiple samples to be mixed and sequenced at the same time.
Clonal amplification: Prior to sequencing, the DNA library must be attached to a solid surface and clonally amplified to increase the signal that can be detected from each target during sequencing. During this process, each unique DNA molecule in the library is bound to the surface of a bead or a flow-cell and PCR amplified to create a set of identical clones. This process is called templating, which is used to add library molecules to beads.
Sequence library: The template is parallelly sequenced on S5 instrument.
Sequencing Analysis: Analysis can be divided into three steps: primary, secondary, and tertiary analysis. Primary analysis is the processing of raw signals from instrument detectors into digitized data or base calls. These raw data are collected during each sequencing cycle. The output of primary analysis is files containing base calls assembled into sequencing reads (BAM files) and their associated quality scores (Phred quality score). Secondary analysis involves read filtering and trimming based on quality, followed by alignment of reads to a reference genome or assembly of reads for novel genomes, and finally by variant calling. Tertiary analysis involves interpreting results and extracting meaningful information from the data.

ANALYSIS SOFTWARE

Torrent Variant Caller plugin – A SNP and indel calling analysis module that is part of the Torrent Suite™ Software and is accessible through the Torrent Browser. The plugin can either be initiated automatically after sequencing data have been generated and bases called, or it can be initiated manually to process previously generated datasets.
Ion Reporter™ Software – A cloud-based software service that provides both variant calling and annotations, designed with traceability features that are essential to researchers who perform sequencing assays. It comprises a suite of bioinformatics tools that streamlines and simplifies analysis, reporting, and archiving of semiconductor sequencing data. Ion Reporter™ Software fast-tracks variant analysis and integrates comprehensive public annotations to reduce the bioinformatics work needed to understand the impact of detected variants and to shorten the time to interpret test results.

LIMITATIONS AND DISCLAIMER

This test was developed, and its performance characteristics was determined at Pathkind Diagnostics Pvt Ltd. This Clinical Report should be interpreted by the Genetic Counsellor/Clinicians. Clinical decision regarding care and treatment of customers should not be solely based on this Test. Treatment decisions are the responsibility of the Clinician/ Hospital.
All investigations have their limitation which is imposed by the limits of sensitivity and specificity of individual assay procedures as well as the quality of the specimen received at Pathkind Diagnostics.

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Large insertions, deletions, duplications, inversions and complex rearrangements cannot be characterized accurately by NGS, as it uses short-read sequencing data. MLPA testing is recommended for the screening of the structural variants.
Isolated laboratory investigations never confirm the final diagnosis of the disease. They only help in arriving at a diagnosis in conjunction with clinical presentation and other related investigations.

REFERENCES

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2. Ranjit Manchanda, Shreeya Patel, Vladimir S Gordeev, Antonis C Antoniou et al. Cost-effectiveness of Population-Based BRCA1, BRCA2, RAD51C, RAD51D, BRIP1, PALB2 Mutation Testing in Unselected General Population Women. J Natl Cancer Inst, 2018 Jul 1;110(7):714-725.
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Note: The performance of this Test has been evaluated at Pathkind Diagnostics Pvt Ltd

This Test is accredited by NABL vide certificate No. MC-3055

#_End of Report_#

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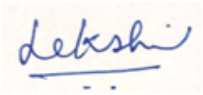

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