Medgenome Labs Ltd
Sy No 94/1C and 94/2, Tower-1, Veerasandra Village, Attibele Hobli, Electronic City, Phase-1, Bangalore, Karnataka, 560100.

MEDGENOME

DNA TEST REPORT

Full Name / Ref No	**K K Chandrika**	Order ID/Sample ID	**1165155/8907680**
Date of Birth / Age	**61 Years**	Gender	**Female**
Parental Sample ID	**NA**	Sample Type	**Peripheral Blood in EDTA (Purple Top)**
Referring Clinician	**Dr. Mahendra Perera Aegle Omics Private Limited Colombo**	Date and time of Sample Collection	**09-01-2025; 12.31 PM**
		Date and time of Sample Receipt	**11-01-2025; 11.45 AM**
		Date and time of Order	**11-01-2025; 12.34 PM**
		Date and time of Report	**28-01-2025; 01.27 PM**
Collection Center/ Partner Lab			
Test Requested	**BRCA1 & BRCA2 deletion/duplication analysis [MGM178]**		

CLINICAL DIAGNOSIS / SYMPTOMS / HISTORY

The patient is a case of lateral quadrant right breast carcinoma. The patient is thus being evaluated for pathogenic copy number variations in the hereditary cancer genes *BRCA1* and *BRCA2*.

RESULTS

NO PATHOGENIC OR LIKELY PATHOGENIC DELETIONS / DUPLICATIONS WAS DETECTED WITHIN THE MLPA ASSAY LIMITS

ADDITIONAL FINDINGS: NO VARIANT(S) OF UNCERTAIN SIGNIFICANCE (VUS) IDENTIFIED

CLINICAL CORRELATION AND VARIANT INTERPRETATION

No deletions or duplications were detected, within the detection limits of Digital MLPA, in *BRCA1* and *BRCA2* genes of this subject.

RECOMMENDATIONS

Genetic counselling is advised.

BACKGROUND

BRCA1 and *BRCA2* are human genes that produce tumor suppressor proteins which helps in repairing damaged DNA and play a very important role in maintaining the stability of the cell's genetic material. When either of these genes is mutated, cells are more likely to develop additional genetic alterations that can lead to cancer. More than 1,800 mutations have been reported in *BRCA1* and *BRCA2* gene which are associated with an increased risk of breast cancer in both men and women, as well as several other types of cancers including prostate, ovarian, pancreatic, fallopian tube, peritoneal, FA-D1 and melanoma. Most of the reported *BRCA1* and *BRCA2* mutations are characterized by deletions, insertions, nonsense mutations, splice variants and an increasing number of large genomic rearrangements. Analysis for large genomic rearrangements which includes large deletion/duplication in *BRCA1*& 2 provides an efficient diagnosis for this disorder and carrier testing in adults with a family history of *BRCA1* &*BRCA2* related disorders.

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TEST METHODOLOGY

DigitalMLPA is a semi-quantitative technique that is used to determine the relative copy numbers for 23 exons for *BRCA1* and 27 exons for *BRCA2* genes. It is like conventional MLPA, is based on the sample DNA-dependent generation of ligated probe products, followed by PCR amplification of ligated probes by a single PCR primer pair. DigitalMLPA generates PCR amplicons that are quantified using Illumina NGS platforms. Sequencing is used to determine the read numbers of each digitalMLPA probe amplicon. Coffalyser digitalMLPA software from MRC Holland for the analysis of digitalMLPA data. Coffalyser digitalMLPA automatically recognizes digitalMLPA sequence reads from FASTQ files and directly uses them for analysis. Coffalyser digitalMLPA then outputs two clear reports for every sample of your experiment indicating both the quality of the run and the aberrations found.

*** Genetic test results are reported based on the recommendations of American College of Medical Genetics (Richards CS et al., Genet Med, 2015), as described below:**

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 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.
Benign	A variant which is known not to be responsible for disease has been detected. Generally no further action is warranted on such variants when detected.
Likely Benign	A 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.
Variant of Uncertain Significance	A variant has been detected, but it 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.

#CNV ratios of below 0.7 or above 1.3 are indicative of a deletion (copy number change from two to one) or duplication (copy number change from two to three), respectively. A CNV ratio of 0.0 indicates a homozygous/hemizygous deletion, 0.35 to 0.65 indicates heterozygous deletion, 1.35 to 1.55 indicates heterozygous duplication and 1.7 to 2.2 indicates homozygous/hemizygous duplication.A ratio between 0.80 to 1.20 indicates a normal copy number status.

DISCLAIMER

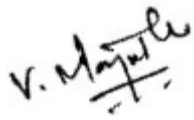
- In most populations, the major cause of genetic defects in the genes covered by the D001 probemix are small (point) mutations, most of which will not be detected by using this probemix.
- Digital MLPA cannot detect any changes that lie outside the target sequence of the probes and will not detect most copy number neutral inversions or translocations. Even when digital MLPA did not detect any aberrations, the possibility remains that biological changes in that gene or chromosomal region do exist but remain undetected.
- Sequence changes (e.g. SNPs, point mutations, small indels) in the target sequence detected by a probe can cause false positive results. Mutations/SNPs (even when >20 nt from the probe ligation site) can reduce the probe read count by preventing ligation of the probe oligonucleotides or by destabilizing the binding of a probe oligonucleotide to the sample DNA.
- The boundaries (positions of start and end) of the deletion/duplication detected, cannot be deciphered by this method.
- The variants in this report are interpreted based on information available in scientific literature at the time of reporting, therefore, an impact and classification of gene variation might change over time with respect to clinical indication. MedGenome cannot be held responsible for this, the clinician can request reanalysis of data on an annual basis at an additional cost.
- Variants in untranslated region, promoters and deep intronic regions are not analyzed in this test.
- Test results are interpreted in the context of clinical findings, family history and other laboratory data. In the absence of detailed accurate clinical or family history of the patient, MedGenome cannot guarantee the accuracy of theinterpretation of results.
- The results may be inaccurate in rare circumstances if the individual tested has undergone bone marrow transplantation or blood transfusion.
- MedGenome is not liable to provide diagnosis, opinion or recommendation related to disease, in any manner.
- MedGenome hereby recommends the Patient and/or the guardians of the Patient to contact clinician for further interpretation of the test results.
- This is a laboratory developed test and the development and the performance characteristics of this test was determined by MedGenome.

Report verified by:

Jeevana Praharsha

Lead Genome Analyst

Report verified by:



Mr. Manjunath V

Senior Manager(Lab Operations)

Report verified by:

Dr. Pragya Gupta MBBS, MD Path, PDF Molecular Genetics (TMCK)

Senior Molecular Pathologist & Clinical Head

APPENDIX-1

Assay covering hereditary Cancer genes:

Chromosomal position (hg38)	Gene	NM sequence and LRG	# probes / # exons in gene	Gene length(kb)	Remarks
13q13.1	***BRCA2***	NM_000059.3 LRG_293	42/27	84.2	Includes one probe for exon 3 ALU insertion c.156_157
17q21.31	***BRCA1***	NM_007294.3 LRG_292	38/23	81.2	Exon numbering different from LRG/NG sequence

---------- End of Report ----------
