CellMax

DNA Genetic Cancer Risk Test

Test Report

CellMax Life

Test Report

CellMax
DNA Genetic
Cancer Risk Test

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Test Report

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1-1. Customer Information

CellMax Sample ID	
Customer First Name	
Customer Last Name	
Date of Birth	
Gender	☐ M ☐ F
Customer Phone Number	
Customer E-mail	
Name of Authorizing Physician	
Date of Sample Receiving	
Date of Report	

Test Report

CellMax
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1-2. Test Report Summary

Summary Result: Positive

Clinically Significant Genetic Mutations Detected

Gene	Mutation	Interpretation
BRCA1	c.5243delG (p.Gly178Valfs)	Associated with Hereditary Breast and Ovarian Cancer Syndrome

The classification and interpretation of all variants identified in the test reflects the current state of scientific and medical understanding at the time the report is generated. The five variant classification categories include pathogenic, likely pathogenic, variant of uncertain significance (VUS), likely benign, and benign. CellMax Life only reports pathogenic variants, which have strong lines of evidence associated with increased cancer risk.

A positive test result for a pathogenic mutation in a gene means that your lifetime risk(s) of developing the associated cancer(s) is significantly higher than an individual who does not have a mutation. **It does not mean that you have cancer or that you will eventually develop cancer in your lifetime.** Likewise, a negative result **does not mean that you do not have cancer, or that you will not develop cancer at some point in your lifetime.**

Comments

Electronic Signatures

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Date

CellMax Life

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1-3. Test Report Details

Result: Pathogenic

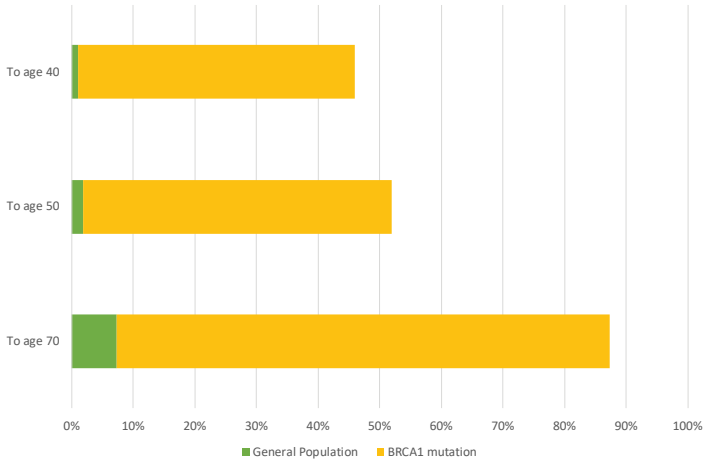
Gene	*BRCA1*	breast cancer type 1 susceptibility protein
RefSeq Transcript ID	**NM_007294.3**	17q21.31; base pairs 43,044,295 to 43,125,483 on chromosome 17.
Mutation	**c.5243delG (p.Gly178Valfs) chr17: 43057086**	Deleterious - Abnormal protein production or function.
Classification	**Pathogenic**	CellMax Life's formal variant classification and medical professional review have shown that the mutation is associated with increased cancer risk and should be regarded as clinically significant. See ClinVar URL below.
Inheritance	**Autosomal Dominant**	In an autosomal dominant disease, one copy of the altered gene in each cell is sufficient to increase an individual's chance of developing cancer.
Clinical Interpretation	**Associated With Increased Cancer Risk**	Females with *BRCA1* mutations may have an increased chance to develop breast cancers, ovarian cancer, and pancreatic cancer.
Family Risk	Family members may be at risk. • Your parents have a 50% chance of having the *BRCA1* mutation. • Your siblings have a 50% chance of having inherited the *BRCA1* mutation. • Each of your children have a 50% chance of inheriting your *BRCA1* mutation. • You may consider sharing your results with family members so they can also be tested for the *BRCA1* mutation that you inherited.	
ClinVar URL		

1-3. Test Report Details

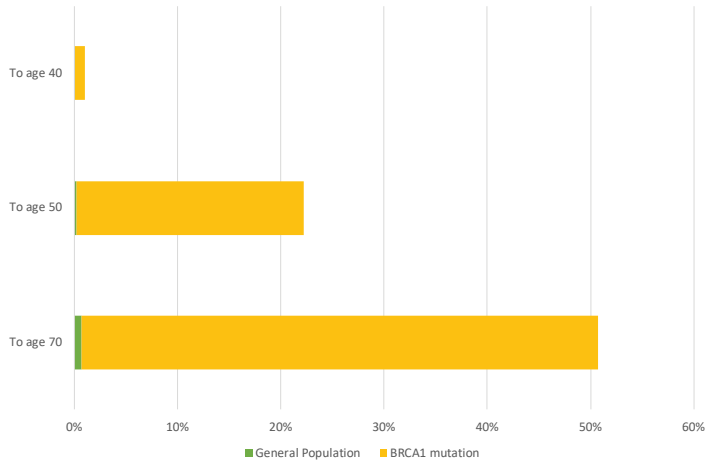
Risk of Cancers With *BRCA1* Mutation

Women with a *BRCA1* mutation have Hereditary Breast and Ovarian Cancer syndrome (HBOC), putting them at a higher risk for breast cancer and ovarian cancer.

Female Breast Cancer [1, 2, 3]



Ovarian Cancer [1, 2, 4]



Elevated Risk of Other Cancers With *BRCA1* Mutation

Women with a *BRCA1* mutation have an elevated risk for pancreatic cancer.

	General Risk	Risk with *BRCA1* Mutation
Pancreatic		
To age 80	1.0%	Elevated [5]
Lifetime	1.3%	Up to 5.3% [4]

References:

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2. Chen S, et al. Characterization of BRCA1 and BRCA2 mutations in a large United States sample. J Clin Oncol. 2006 24:863-71. PMID: 16484695
3. Antoniou A, Pharoah PDP, Narod S, et al. Average Risks of Breast and Ovarian Cancer Associated with BRCA1 or BRCA2 Mutations Detected in Case Series Unselected for Family History: A Combined Analysis of 22 Studies. American Journal of Human Genetics. 2003
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1-4. List of Cancers / Tumors Tested

Cancer / Tumor	Gene(s) Correlation	Pathogenic Gene Mutation Detected
Breast	*ATM, BARD1, **BRCA1**, BRCA2, BRIP1, CDH1, CHEK2, NBN, NF1, PALB2, PPM1D, PTEN, RAD51C, STK11, TP53*	Yes
Ovaries	***BRCA1**, BRCA2, BRIP1, DICER1, EPCAM, MLH1, MSH2, MSH6, PALB2, PMS2, PPM1D, RAD51C, RAD51D, STK11, TP53*	Yes
Endometrium (Uterine)	*EPCAM, MLH1, MSH2, MSH6, PMS2, PTEN, STK11, TP53*	No
Myometrium (Uterine)	*FH*	No
Prostate Gland	***BRCA1**, BRCA2, CHEK2, HOXB13, NBN, TP53*	Yes
Stomach	*APC, BMPR1A, CDH1, EPCAM, KIT, MLH1, MSH2, MSH6, PMS2, SMAD4, STK11*	No
Large Bowel and Rectum (Colorectal)	*APC, BLM, BMPR1A, CDH1, CHEK2, EPCAM, KIT, MLH1, MSH2, MSH6, MUTYH, PMS1, PMS2, PTEN, SMAD4, STK11, TP53*	No
Lung and Pleura	*BAP1, DICER1, EGFR*	No
Small Intestines	*KIT, MLH1, MSH2, MSH6, SDHB, SDHC, SDHD, STK11*	No
Esophagus	*FANCA, FANCB, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCI, FANCL, FANCM, RHBDF2*	No
Urinary Tract and Bladder	*HRAS, MLH1, MSH2, MSH6*	No

1-4. List of Cancers / Tumors Tested

Cancer / Tumor	Gene(s) Correlation	Pathogenic Gene Mutation Detected
Exocrine Pancreas	*APC, ATM, BMPR1A, **BRCA1**, BRCA2, CDK4, CDKN2A, EPCAM, MLH1, MSH2, MSH6, PALB2, PMS2, SMAD4, STK11, TP53*	Yes
Endocrine Pancreas	*MEN1, NF1, VHL*	No
Kidneys	*BAP1, BUB1B, CEP57, DICER1, DIS3L2, FH, FLCN, MET, PTEN, SDHB, SDHC, SDHD, SMARCB1, TSC1, TSC2, VHL, WT1*	No
Cervix	*STK11*	No
Skin	*BAP1, CDK4, CDKN2A, DDB2, ERCC2, ERCC3, ERCC4, ERCC5, NF2, PTEN, TP53, XPA, XPC*	No
Bone	*EXT1, EXT2, RECQL4, TP53*	No
Thyroid Gland	*APC, CHEK2, DICER1, MEN1, PRKAR1A, PTEN, RET, TP53*	No
Liver	*APC, HNF1A*	No
Soft Tissue	*RB1, WRN*	No
Miscellaneous Endocrine Glands	*CDC73, FH, MAX, MEN1, RET, SDHAF2, SDHB, SDHC, SDHD, TMEM127, VHL*	No
Blood	*CEBPA, GATA2, PRF1, RUNX1, SBDS*	No

1-4. List of Cancers / Tumors Tested

Cancer / Tumor	Gene(s) Correlation	Pathogenic Gene Mutation Detected
Head and Neck	*CDK4, CYLD, FANCA, FANCB, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCI, FANCL, FANCM, SLX4*	No
Central Nervous System	*AIP, APC, CDKN1C, CDKN2A, DICER1, GPC3, MLH1, MSH2, MSH6, NBN, NF2, PMS2, PRKAR1A, PTCH1, PTEN, SMARCA4, SMARCB1, SUFU, TP53, TSC2*	No
Peripheral Nervous System	*ALK, EZH2, FH, NF1, NF2, NSD1, PHOX2B, SDHAF2, SDHB*	No

SECTION 2

2-1. About the Test

2-2. References

Test Report

CellMax
DNA Genetic
Cancer Risk Test

2-1. About the Test

CellMax Life has developed a next-generation sequencing-based test for hereditary cancer susceptibility genes. The assay uses advanced next-generation sequencing (SMSEQ™) to sequence the coding sequences and intron/exon boundaries for the genes of interest. The assay has a high-degree of analytical sensitivity and specificity. Validation using industry standard methods yielded an accuracy of >99.99%. The genetic panel was curated by medical doctors to include 98 genes reported in the literature as being associated with major cancers. A complete list of genes is part of this test report.

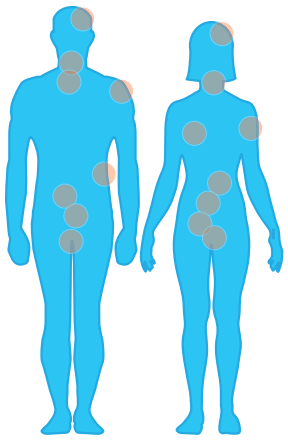
This test was developed and its performance characteristics determined by CellMax Life, a clinical laboratory certified under Clinical Laboratory Improvement Amendments (CLIA) to perform high-complexity testing. This test is used for clinical purposes, and should not be regarded as investigational or for research.

Genes Tested

AIP	*ALK*	*APC*	*ATM*	*BAP1*	*BARD1*	*BLM*	*BMPR1A*	*BRCA1*
BRCA2	*BRIP1*	*BUB1B*	*CDC73*	*CDH1*	*CDK4*	*CDKN1C*	*CDKN2A*	*CEBPA*
CEP57	*CHEK2*	*CYLD*	*DDB2*	*DICER1*	*DIS3L2*	*EGFR*	*EPCAM*	*ERCC2*
ERCC3	*ERCC4*	*ERCC5*	*EXT1*	*EXT2*	*EZH2*	*FANCA*	*FANCB*	*FANCC*
FANCD2	*FANCE*	*FANCF*	*FANCG*	*FANCI*	*FANCL*	*FANCM*	*FH*	*FLCN*
GATA2	*GPC3*	*HNF1A*	*HOXB13*	*HRAS*	*KIT*	*MAX*	*MEN1*	*MET*
MLH1	*MHS2*	*MSH6*	*MUTYH*	*NBN*	*NF1*	*NF2*	*NSD1*	*PALB2*
PHOX2B	*PMS1*	*PMS2*	*PPM1D*	*PRF1*	*PRKAR1A*	*PTCH1*	*PTEN*	*RAD51C*
RAD51D	*RB1*	*RECQL4*	*RET*	*RHBDF2*	*RUNX1*	*SBDS*	*SDHAF2*	*SDHB*
SDHC	*SDHD*	*SLX4*	*SMAD4*	*SMARCA4*	*SMARCB1*	*STK11*	*SUFU*	*TMEM127*
TP53	*TSC1*	*TSC2*	*VHL*	*WT1*	*WRN*	*XPA*	*XPC*	

Cancer / Tumor Risks Tested

Breast	Ovaries	Endometrium, Uterine
Myometrium, Uterine	Prostate Gland	Stomach
Large Bowel and Rectum	Lung and Pleura	Small Intestines
Esophagus	Urinary Tract and Bladder	Exocrine Pancreas
Endocrine Pancreas	Kidneys	Cervix
Skin	Bone	Thyroid Gland
Liver	Soft Tissue	Miscellaneous Endocrine Glands
Blood	Head and Neck	Central Nervous System
Peripheral Nervous System		



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Details About Mutations and Variants

Genetic Variants

All persons carry genetic variants inherited from their parents. A variant can be used to describe a change in a DNA sequence that may be pathogenic, likely pathogenic, unknown significance, likely benign, or benign. Most variants do not cause an increase in the risk of cancer or other disease. The classification and interpretation of all variants identified in the test reflects the current state of scientific and medical understanding at the time the report is generated. Variants are classified by pathogenicity by taking into account the reported variant, and the allelic frequencies from population studies and clinical databases (e.g. 1000 Genomes, ClinVar). A positive test result indicates that an individual has inherited a pathogenic mutation in specific genes and, therefore, has an increased risk of developing certain cancers. It is important to understand that a positive test result does not necessarily mean that the individual will actually develop cancer over their lifetime. Some individuals who inherit pathogenic mutations will never develop the associated cancer(s). A negative test result indicates that an individual has not inherited a pathogenic mutation in any of the genes tested, but does not eliminate the lifetime risk of developing certain cancers.

Pathogenic Variants

Certain mutations in certain genes are associated with an increased risk for cancers and/or hereditary syndromes. These mutations are associated with the potential to alter medical intervention. A pathogenic variant directly contributes to the development of cancer. The variant has strong lines of evidence that associates it with significantly increased cancer risk and necessary clinical action.

Likely Pathogenic Variants

A likely pathogenic variant is very likely to contribute to the development of cancer. The variant has fewer strong lines of evidence that associates it with significantly increased cancer risk.

Uncertain Significance Variants (VUS)

A variant of uncertain significance does not have enough information at this time to support a more definitive classification. There is insufficient evidence to determine if the variant is associated with increased cancer risk.

Likely Benign

A likely benign variant is not expected to have a major effect on cancer. However, additional evidence is needed to confirm this assertion.

Benign

A benign variant has strong lines of evidence that does not associate it with an increased cancer risk.

Test Limitations

Inherited mutations in certain genes are associated with hereditary cancer syndromes or increased risk to various cancer types. The test interrogates and reports single nucleotide variants, insertions, and deletions in genomic DNA. Large scale genomic rearrangements, copy number variants, as well as structural changes are not detected. CellMax Life only reports pathogenic variants, which have strong lines of evidence associated with increased cancer risk.

The absence of a pathogenic mutation does not eliminate an individual's risk of developing cancer, as cancer can be caused by, but not limited to, both inherited and acquired genetic mutations. Sources of acquired genetic mutations include various factors such as aging, environment, and lifestyle choices. The test is not recommended for new bone marrow transplant recipients.

2-2. References

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7. The Cancer Genome Atlas. Cancers Selected for Study. Accessed at http : //Cancergenome.nih.gov/cancersselected on October 14. 2013.
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9. Garber JE, Offit K (2005) Hereditary cancer predisposition syndromes. J Clin Oncol 23:276-29
10. Hampel H, Sweet K, Westman JA, et al. (2004) Referral for cancer genetics consultation : A review and compilation of risk assessment criteria. J Med Genet 41:81-91

Disclaimer

DNA studies do not constitute a definitive test for any disease conditions in an individual. This test was developed and its performance characteristics determined by CellMax Life. Clinical decisions regarding care and treatment of customers should not be solely based on this test. How this information is used to guide customer care is the responsibility of the physician.

The CellMax Life test is designed to assist health care practitioners in providing additional clinical information. The information therein should not be relied upon as being complete or accurate, nor should it be considered as inclusive of all proper treatments or methods of care or as a statement of the standard of care. Medical knowledge develops rapidly and new evidence may emerge between the time information is developed to when it is published or read.

Genetics is about probabilities, not certainties. It is important to realize that many variables impact our genes so the outcome is not certain even if we have a known genetic risk factor. An unfavorable mutation means you are much more likely to be affected by that gene than others who do not carry the same mutation. But the tremendous benefit of genetic testing is that you can influence the gene by the choices you make in your lifestyle, diet, nutrition, supplements, exercise and even your outlook. Genes can be turned on and off by our lifestyle choices and if you have an unfavorable mutation you can still influence a lot of control over its expression.

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