Genetic Result - Integrated BRACAnalysis®
BRCA1 and *BRCA2* Analysis

BRACAnalysis® Powered by myVision

RECEIVING HEALTHCARE PROVIDER	SPECIMEN		PATIENT	
Test HCP, MD	Specimen Type:	**Blood**	Name:	**Pt Last Name, Pt First Name**
Test Medical Center	Draw Date:	**Jun 09, 2016**	Date of Birth:	
123 Main St	Accession Date:	**Jun 09, 2016**	Patient ID:	**Patient id**
Testville, TX 55555	Report Date:	**Jun 14, 2016**	Gender:	**Female**
			Accession #:	**07001268-BLD**
			Requisition #:	**7001268**

RESULT: POSITIVE - CLINICALLY SIGNIFICANT MUTATION IDENTIFIED

Note: "CLINICALLY SIGNIFICANT," as defined in this report, is a genetic change that is associated with the potential to alter medical intervention.

GENE	MUTATION	INTERPRETATION
BRCA2	**c.xxxxxxxxxxxx** Heterozygous	**High Cancer Risk** This patient has Hereditary Breast and Ovarian Cancer syndrome (HBOC).

DETAILS ABOUT: *BRCA2* c.xxxxxx: NM_000059.3; (aka: xxxxx)

Functional Significance: Deleterious - Abnormal Protein Production and/or Function

The heterozygous germline *BRCA2* mutation c.xxxxx is predicted to result in the premature truncation of the *BRCA2* protein at amino acid position xxxx (p.xxxxx).

Clinical Significance: High Cancer Risk

This mutation is associated with increased cancer risk and should be regarded as clinically significant.

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

Details About Non-Clinically Significant Variants: All individuals carry DNA changes (i.e., variants), and most variants do not increase an individual's risk of cancer or other diseases. When identified, variants of uncertain significance (VUS) are reported. Likely benign variants (Favor Polymorphisms) and benign variants (Polymorphisms) are not reported and available data indicate that these variants most likely do not cause increased cancer risk. Present evidence does not suggest that non-clinically significant variant findings be used to modify patient medical management beyond what is indicated by the personal and family history and any other clinically significant findings.

Variant Classification: Myriad's myVision™ Variant Classification Program performs ongoing evaluations of variant classifications. In certain cases, healthcare providers may be contacted for more clinical information or to arrange family testing to aid in variant classification. When new evidence about a variant is identified and determined to result in clinical significance and management change, that information will automatically be made available to the healthcare provider through an amended report.

ADDITIONAL INFORMATION

GENES ANALYZED

Unless otherwise noted sequencing and large rearrangement analyses were performed on the following genes:

BRCA1, *BRCA2*

Indication for Testing: It is our understanding that this individual was identified for testing due to a personal or family history suggestive of a hereditary predisposition for cancer.

Associated Cancer Risks and Clinical Management: If a clinically significant mutation is identified, please see the management tool associated with this report for a summary of cancer risk and professional society medical management guidelines that may be useful in developing a plan for this patient. Testing of other family members may assist in the interpretation of this patient's test result.

Analysis Description: The Technical Specifications summary (https://www.myriadpro.com/documents-and-forms/technical-specifications/) describes the analysis, method, performance, nomenclature, and interpretive criteria of this test. Current testing technologies are unable to definitively determine whether a variant is germline or somatic in origin, which may significantly impact risk estimates and medical management; therefore, these results should be correlated with this patient's personal and family history. The interpretation of this test may also be impacted if the patient has a hematologic malignancy or an allogeneic bone marrow transplant.

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THE CLASSIFICATION AND INTERPRETATION OF ALL VARIANTS IDENTIFIED IN THIS ASSAY REFLECTS THE CURRENT STATE OF MYRIAD'S SCIENTIFIC UNDERSTANDING AT THE TIME THIS REPORT WAS ISSUED. VARIANT CLASSIFICATION AND INTERPRETATION MAY CHANGE FOR A VARIETY OF REASONS, INCLUDING BUT NOT LIMITED TO, IMPROVEMENTS TO CLASSIFICATION TECHNIQUES, AVAILABILITY OF ADDITIONAL SCIENTIFIC INFORMATION, AND OBSERVATION OF A VARIANT IN MORE PATIENTS.

Please contact Myriad Medical Services at 1-800-469-7423 X 3850 to discuss any questions regarding this result.

This **Authorized Signature** pertains to this laboratory report:

Benjamin B. Roa, PhD
Diplomate ABMG
Laboratory Director

Johnathan M. Lancaster, MD, PhD
Diplomate FACOG, FACS
Chief Medical Officer

These test results should only be used in conjunction with the patient's clinical history and any previous analysis of appropriate family members. The patient's clinical history and test results should not be disclosed to a third party, unless related to treatment or payment for treatment, without the patient's express written authorization. It is strongly recommended that these results be communicated to the patient in a setting that includes appropriate counseling. This test was developed and its performance characteristics determined by Myriad Genetic Laboratories. It has not been cleared or approved by the U.S. Food and Drug Administration (FDA). The FDA has determined that clearance or approval for laboratory-developed tests is not required.

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Management Tool - Integrated BRACAnalysis®
BRCA1 and *BRCA2* Analysis

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GENETIC TEST RESULTS SUMMARY INFORMATION

RESULT: POSITIVE - CLINICALLY SIGNIFICANT MUTATION IDENTIFIED

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

GENE	MUTATION	THIS GENETIC TEST RESULT IS ASSOCIATED WITH THE FOLLOWING CANCER RISKS:
BRCA2	**c.XXXXXXXXXXXX** Heterozygous	**HIGH RISK:** Female Breast, Ovarian, Pancreatic
		ELEVATED RISK: Melanoma

OVERVIEW

Hereditary Breast and Ovarian Cancer syndrome (HBOC):

- This patient has been found to have a mutation in the *BRCA2* gene. Individuals with mutations in *BRCA2* have a condition called Hereditary Breast and Ovarian Cancer syndrome (HBOC).
- Women with HBOC have a risk for breast cancer that is greatly increased over the 12.5% lifetime risk for women in the general population of the United States.
- Women with HBOC also have high risks for ovarian, fallopian tube, and primary peritoneal cancer.
- Men with HBOC due to mutations in *BRCA2* have a high risk for breast cancer and an elevated risk for prostate cancer. The increase in prostate cancer risk is most significant at younger ages.
- Male and female patients with HBOC due to a mutation in *BRCA2* also have a high risk for pancreatic cancer and an elevated risk for melanoma.
- Although there are high cancer risks for patients with HBOC, there are interventions that have been shown to be effective at reducing many of these risks. Guidelines from the National Comprehensive Cancer Network (NCCN) for the medical management of patients with HBOC are listed below. It is recommended that patients with *BRCA2* mutations and a diagnosis of HBOC be managed by a multidisciplinary team with experience in the prevention and treatment of the cancers associated with HBOC.

WHAT ARE THE PATIENT'S GENE-RELATED CANCER RISKS?

If more than one gene mutation increases a specific cancer risk (e.g., breast), only the highest cancer risk is shown. If this patient has more than one gene mutation, risks may be different, as this analysis does not account for possible interactions between gene mutations.

CANCER TYPE	CANCER RISK	RISK FOR GENERAL POPULATION	RELATED TO

Management Tool - Integrated BRACAnalysis®

Name: **Pt Last Name, Pt First Name** DOB: Accession #: **07001268-BLD** Report Date: **Jun 14, 2016**

CANCER TYPE	CANCER RISK	RISK FOR GENERAL POPULATION	RELATED TO
FEMALE BREAST			
To age 50	23%-28%	1.9%	*BRCA2*
To age 70	43%-84%	7.3%	*BRCA2*
Second primary within 5 years of first breast cancer diagnosis	12%	2%	*BRCA2*
OVARIAN			
To age 50	0.4%-4%	0.2%	*BRCA2*
To age 70	16.5%-27%	0.7%	*BRCA2*
Ovarian cancer within 10 years of a breast cancer diagnosis	6.8%	<1.0%	*BRCA2*
PANCREATIC			
To age 80	7%, or higher if there is a family history of pancreatic cancer.	1%	*BRCA2*
MELANOMA			
To age 80	Elevated risk	1.6%	*BRCA2*

WHAT MANAGEMENT FOR CANCER RISKS SHOULD BE CONSIDERED?

This overview of clinical management guidelines is based on this patient's genetic test results. Unless otherwise stated, medical management guidelines are limited to those issued by the National Comprehensive Cancer Network (NCCN). The reference provided should always be consulted for more details. If management for a specific cancer (e.g. breast) is available due to multiple mutations, only the most aggressive management is shown. Only guidelines for the patient's long-term care related to cancer prevention are included.

No information is provided related to treatment of a previous or existing cancer or polyps. These recommendations may require modification based on the patient's personal medical history, surgeries and other treatments. Patients with a personal history of cancer, benign tumors or pre-cancerous findings may be candidates for long term surveillance and risk reduction strategies beyond what is necessary for the treatment of their initial diagnosis. Any discussion of medical management options is for general information purposes only and does not constitute a recommendation. While genetic testing and medical society guidelines provide important and useful information, medical management decisions should be made in consultation between each patient and his or her healthcare provider.

PROCEDURE	AGE TO BEGIN	FREQUENCY (Unless otherwise indicated by findings)	RELATED TO

Management Tool - Integrated BRACAnalysis®

Name: **Pt Last Name, Pt First Name** DOB: Accession #: **07001268-BLD** Report Date: **Jun 14, 2016**

PROCEDURE	AGE TO BEGIN	FREQUENCY (Unless otherwise indicated by findings)	RELATED TO
FEMALE BREAST			
Breast awareness - Women should be familiar with their breasts and promptly report changes to their healthcare provider. Periodic, consistent breast self-examination (BSE) may facilitate breast awareness.[1]	18 years	NA	*BRCA2*
Clinical breast examination[1]	25 years	Every 6 to 12 months	*BRCA2*
Breast MRI and/or Mammography[1]	Age 25 for MRI (preferred) or mammography. Age 30 for both MRI and mammography. Individualize to a younger age if a relative has been diagnosed younger than age 30.	Annually	*BRCA2*
Consider investigational screening studies within clinical trials.[1]	Individualized	NA	*BRCA2*
Consider risk-reducing mastectomy.[1]	Individualized	NA	*BRCA2*
Consider options for breast cancer risk reduction agents (i.e. tamoxifen).[1]	Individualized	NA	*BRCA2*
OVARIAN			
Bilateral salpingo-oophorectomy[1]	35 to 40 years, upon completion of childbearing, or 40 to 45 for women who have already maximized their breast cancer risk prevention	NA	*BRCA2*
Consider transvaginal ultrasound and CA-125 measurement. Consider investigational screening studies within clinical trials.[1]	30 to 35 years	Individualized	*BRCA2*
Consider options for ovarian cancer chemoprevention (i.e. oral contraceptives).[1]	Individualized	NA	*BRCA2*
PANCREATIC			
Consider available options for pancreatic cancer screening, including the possibility of endoscopic ultrasonography (EUS) and MRI/magnetic resonance cholangiopancreatography (MRCP). It is recommended that patients who are candidates for pancreatic cancer screening be managed by a multidisciplinary team with experience in the screening for pancreatic cancer, preferably within research protocols.[2]	Individualized	NA	*BRCA2*

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PROCEDURE	AGE TO BEGIN	FREQUENCY (Unless otherwise indicated by findings)	RELATED TO
MELANOMA			
Consider whole-body skin and eye examinations.[1]	Individualized	NA	*BRCA2*

1. Daly M et al. NCCN Clinical Practice Guidelines in Oncology®: Genetic/Familial High-Risk Assessment: Breast and Ovarian. V 1.2016. Feb 18. Available at http://www.nccn.org.
2. Canto MI, et al. International Cancer of the Pancreas Screening (CAPS) Consortium summit on the management of patients with increased risk for familial pancreatic cancer. Gut. 2013 62:339-47. PMID: 23135763.

Notes for Personalized Management: _____

INFORMATION ON HOW CANCER RISKS AND MANAGEMENT ARE DETERMINED

The Management Tool provides cancer risk levels and management recommendations based on analysis of the genetic results (see Genetic Result). Additional details and references for cancer risks and management recommendations can be found on myriadpro.com/gene-table.

- A comprehensive risk assessment may include other aspects of the patient's personal/family medical history, as well as lifestyle, environment and other factors.
- No management recommendations are provided related to treatment of a previous or existing cancer or polyps. The recommendations provided may require modification based on the patient's personal medical history, surgeries and other treatments. Patients with a personal history of cancer, benign tumors or pre-cancerous findings may be candidates for long term surveillance and risk reduction strategies beyond what is necessary for the treatment of their initial diagnosis.
- Patients who have a clinical diagnosis of a genetic cancer syndrome (e.g., Lynch syndrome) may have different management recommendations than provided. Management should be personalized based on all known clinical diagnoses.
- The Genetic Test Result Summary includes: female breast, male breast, colorectal, endometrial, gastric, ovarian, pancreatic and prostate cancers, and melanoma. In this summary a gene associated cancer risk is described as "High Risk" for a cancer type if all of the following conditions are met: the absolute risk of cancer is approximately 5% or higher, the increase in risk over the general population is approximately 3-fold or higher, and there is significant data from multiple studies supporting the cancer risk estimate. A gene is described as "Elevated Risk" for a cancer type if there is sufficient data to support an increase in cancer risk over the general population risk, but not all criteria for "High Risk" are met.

INFORMATION FOR FAMILY MEMBERS

Family members should talk to their healthcare providers about hereditary cancer testing to help define their own risk and assist in the interpretation of this patient's genetic test result.

- This patient's relatives are at risk for carrying the same mutation(s) and associated cancer risks as this patient. Cancer risks for females and males who have this/these mutation(s) are provided below.
- **Family members should talk to a healthcare provider about genetic testing.** Close relatives such as parents, children, brothers, and sisters have the highest chance of having the same mutation(s) as this patient. Other more distant relatives such as cousins, aunts, uncles, and grandparents also have a chance for carrying the same mutation(s). Testing of at-risk relatives can identify those family members with the same mutation(s) who may benefit from surveillance and early intervention. More resources for family testing are available at MySupport360.com.
- In rare instances, an individual may inherit mutations in both copies of the *BRCA2* gene, leading to the condition Fanconi Anemia, Complementation Group D1 (FANCD1). This condition is rare and includes physical abnormalities, growth retardation, progressive bone marrow failure and a high risk for cancer. The children of this patient are at risk of inheriting FANCD1 only if the other parent is also a carrier of a *BRCA2* mutation. Screening the spouse/partner of this patient for *BRCA2* mutations may be appropriate.

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CANCER RISK FOR *BRCA2* CLINICALLY SIGNIFICANT MUTATION

CANCER TYPE	CANCER RISK	RISK FOR GENERAL POPULATION
FOR FEMALE RELATIVES		
FEMALE BREAST		
To age 50	23%-28%	1.9%
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To age 70	16.5%-27%	0.7%
Ovarian cancer within 10 years of a breast cancer diagnosis	6.8%	<1.0%
FOR MALE RELATIVES		
MALE BREAST		
To age 70	6.8%	<0.1%
PROSTATE		
To age 70	20%	8.2%
FOR FEMALE AND MALE RELATIVES		
PANCREATIC		
To age 80	7%, or higher if there is a family history of pancreatic cancer.	1%
MELANOMA		
To age 80	Elevated risk	1.6%

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END OF MANAGEMENT TOOL

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DETAILS ABOUT: *BRCA2* c.xxxxxx: NM_000059.3; (aka: xxxxx)

Functional Significance: Deleterious - Abnormal Protein Production and/or Function

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This mutation is associated with increased cancer risk and should be regarded as clinically significant.

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

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ADDITIONAL INFORMATION

GENES ANALYZED

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BRCA1, *BRCA2*

Indication for Testing: It is our understanding that this individual was identified for testing due to a personal or family history suggestive of a hereditary predisposition for cancer.

Associated Cancer Risks and Clinical Management: If a clinically significant mutation is identified, please see the management tool associated with this report for a summary of cancer risk and professional society medical management guidelines that may be useful in developing a plan for this patient. Testing of other family members may assist in the interpretation of this patient's test result.

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