51568079

Integrated BRAC*Analysis*® with Myriad myRisk™ Hereditary Cancer

myRisk Genetic Result

MYRIAD myRisk™ Hereditary Cancer | Powered by myVision™

RECEIVING HEALTHCARE PROVIDER	SPECIMEN		PATIENT	
Test Medical Center	Specimen Type:	**Blood**	Name:	**Pt Last Name, Pt First Name**
123 Main St	Draw Date:	**Aug 06, 2013**	Date of Birth:	
Testville, TX 55555	Accession Date:	**Aug 06, 2013**	Patient ID:	**Patient Id**
	Report Date:	**Jul 28, 2014**	Gender:	**Female**
			Accession #:	**07000606-BLD**
			Requisition #:	**7000606**

ORDERING PHYSICIAN: **Test HCP, MD**

RESULT: CARRIER FOR A CLINICALLY SIGNIFICANT MUTATION OF A RECESSIVE CONDITION

GENE	MUTATION	INTERPRETATION
MUTYH	**c.xxxx (p.xxxx*)** Heterozygous	**CARRIER - Elevated Cancer Risk** This patient has MUTYH-associated Colon Cancer Risk.

DETAILS ABOUT: ***MUTYH*** **c.xxxx (p.xxxx*): NM_001128425.1; (aka: c.xxxx (p.xxxx*), xxxx (xxxx)**

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

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

Clinical Significance: Elevated 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:

APC, *ATM*, *BARD1*, *BMPR1A*, *BRCA1*, *BRCA2*, *BRIP1*, *CDH1*, *CDK4*, *CDKN2A*, *CHEK2*, *EPCAM* (large rearrangement only), *MLH1*, *MSH2*, *MSH6*, *MUTYH*, *NBN*, *PALB2*, *PMS2*, *PTEN*, *RAD51C*, *RAD51D*, *SMAD4*, *STK11*, *TP53*.

** Other genes not analyzed with this test may also be associated with cancer.

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: Please see the "myRisk 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 based on test results and reported personal/family history, if applicable. Testing of other family members may assist in the interpretation of this patient's test result.

Analysis Description: The Technical Specifications summary (MyriadPro.com/myRisk) describes the analysis, method, performance, nomenclature, and interpretive criteria of this test. The classification and interpretation of all variants identified in this assay reflects the current state of scientific understanding at the time this report was issued, and may change as new scientific information becomes available. The interpretation of this test may be impacted if the patient has a hematologic malignancy or an allogeneic bone marrow transplant.

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myRisk Genetic Result

Name: **Pt Last Name, Pt First Name** DOB: Accession #: **07000606-BLD** Report Date: **Jul 28, 2014**

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

Richard J. Wenstrup, MD
Diplomate ABMG
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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myRisk Management Tool

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RECEIVING HEALTHCARE PROVIDER

Test Medical Center
123 Main St
Testville, TX 55555

SPECIMEN

Specimen Type:	**Blood**
Draw Date:	**Aug 06, 2013**
Accession Date:	**Aug 06, 2013**
Report Date:	**Jul 28, 2014**

PATIENT

	Pt Last Name, Pt First Name
Date of Birth:	
Patient ID:	**Patient Id**
Gender:	**Female**
Accession #:	**07000606-BLD**
Requisition #:	**7000606**

ORDERING PHYSICIAN: **Test HCP, MD**

GENETIC TEST RESULTS SUMMARY INFORMATION

RESULT: CARRIER FOR A CLINICALLY SIGNIFICANT MUTATION OF A RECESSIVE CONDITION

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

GENE	MUTATION	THIS GENETIC TEST RESULT IS ASSOCIATED WITH THE FOLLOWING CANCER RISKS:
MUTYH	**c.xxxx (p.xxxx*)** Heterozygous	**ELEVATED RISK:** Colorectal

PERSONAL/FAMILY HISTORY SUMMARY AND MANAGEMENT INFORMATION

FAMILY MEMBER	CANCER / CLINICAL DIAGNOSIS	AGE AT DIAGNOSIS
Patient	None	
Aunt Maternal	Breast, Invasive	45
Uncle Maternal	Colorectal	55

This information was provided by a qualified healthcare provider on the test request form and was not verified by Myriad. Family members listed as "other" are not included in personal/family history assessment.

* **BEYOND THE GENETIC RESULT, NO MODIFIED MANAGEMENT GUIDELINES IDENTIFIED; OTHER CLINICAL FACTORS MAY INFLUENCE INDIVIDUALIZED MANAGEMENT**

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myRisk Management Tool

Name: **Pt Last Name, Pt First Name** DOB: Accession #: **07000606-BLD** Report Date: **Jul 28, 2014**

OVERVIEW

MUTYH-associated Colon Cancer Risk:

- This patient has been found to have a mutation in only one copy of the *MUTYH* gene (monoallelic mutation). Individuals with a single *MUTYH* mutation may have a small increased risk for colon cancer. This increase in risk seems to be seen most consistently in patients who have a close relative (parent, brother, sister or child) who has had colon cancer, with increases in risk that are roughly equal to those associated with family history alone. Therefore, medical management for patients with a single *MUTYH* mutation is based on family history guidelines rather than the genetic test results.
- Individuals with mutations in both of their copies of the *MUTYH* gene (biallelic mutations) have a condition known as *MUTYH*-associated polyposis (MAP), which is associated with a high risk for cancer. This patient does not have a diagnosis of MAP, but may have relatives who are at risk for this condition. Please see the Information for Family Members section below for details.

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
COLORECTAL			
To age 80	3.4% to 10%	3.4%	*MUTYH Monoallelic*

WHAT MANAGEMENT FOR CANCER RISKS SHOULD BE CONSIDERED?

This overview of clinical management guidelines is based on this patient's personal and family history and 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 causes (e.g. a mutation and a family history, or multiple mutations in different genes), 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
COLORECTAL			
Currently there are no specific medical management guidelines for colorectal cancer risk in carriers of a single MUTYH mutation. Therefore, screening should be based on any other gene mutations present or any family history of colorectal cancer or adenomas.[1,2]	Individualized	Individualized	*MUTYH Monoallelic*

1. Burt RW et al. NCCN Clinical Practice Guidelines in Oncology® Colorectal Cancer Screening. V 2.2013. July 1. Available at http://www.nccn.org.
2. Provenzale D, et al. NCCN Clinical Practice Guidelines in Oncology® Genetic/Familial High-Risk Assessment: Colorectal V 1.2014. Feb 24. Available at http://www.nccn.org.

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myRisk Management Tool

Name: **Pt Last Name, Pt First Name** DOB: Accession #: **07000606-BLD** Report Date: **Jul 28, 2014**

Notes for Personalized Management: _____

INFORMATION ON HOW CANCER RISKS AND MANAGEMENT ARE DETERMINED

The myRisk Management Tool provides cancer risk levels based on analysis of genetic test results (see myRisk Genetic Result) and management recommendations based on a combined analysis of genetic test results and, when possible, personal/family cancer history. Additional details can be found on MyriadPro.com/myRisk.

- A comprehensive risk assessment may include other aspects of the patient's personal/family medical history, as well as lifestyle, environment and other factors.
- Changes in personal/family history or additional data regarding specific genes/mutations may affect the cancer risk estimates and management recommendations within this report. Personal/family history should be updated with a healthcare provider on a regular basis.
- Management recommendations are provided for personal/family history of colorectal adenomas, breast, colorectal, melanoma, pancreatic, and prostate cancers. Assessment is based on information provided on the test request form for the patient as well as first and second degree relatives. Analysis of third degree relatives for relevant cancers may be included if sufficient information is provided. Assessment for Amsterdam II Criteria for Lynch syndrome may not be complete in certain cases due to Myriad's limited understanding of the family structure. The Claus model is used to determine when women are estimated to have a greater than 20% lifetime risk for breast cancer based on family history (Claus EB, Risch N, Thompson WD. Cancer 1994; Feb 1;73(3):643-51). Unaffected women meeting this threshold will receive appropriate guideline-based breast management recommendations. Additional family history assessment may be required. African American ethnicity, when reported on the test request form, is used in assessment for prostate cancer management. Cancer risks and related management are included based on the gender provided. When personal and family history assessment could not be provided in this result (e.g., Single Site testing, insufficient history for analysis), the patient risk and/or management recommendations may deviate from what has been provided within this report. Please contact Myriad Medical Services at 1-800-469-7423 X 3850 for more information.
- 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.
- This patient carries one or more *MUTYH* clinically actionable mutations. This patient's relatives are at risk for carrying one or more *MUTYH* clinically actionable mutations. *MUTYH* mutations are associated with either *MUTYH*-associated Polyposis syndrome (MAP; 43%-100% colorectal cancer risk to age 80; 5% small bowel cancer risk to age 80) or *MUTYH*-associated Colon Cancer Risk (3.4%-10% colorectal cancer risk to age 80) depending on whether one or both *MUTYH* gene copies carry a clinically actionable mutation. Genetic testing may be appropriate for close family members to determine whether or not they are at a significantly increased risk for colorectal and other cancers.

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END OF MYRISK MANAGEMENT TOOL

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