

Specimen ID:

Control ID:

Acct#:

Phone:

**TESTING**

**Patient Details**

DOB:  
 Age (yyy/mm/dd):  
 Gender:  
 Patient ID:

**Specimen Details**

Date collected:  
 Date received:  
 Date entered:  
 Date reported:

**Physician Details**

Ordering:  
 Referring:  
 ID:  
 NPI:

**POSITIVE**

At least one clinically significant variant was detected.

**RESULTS AND INTERPRETATION**

+	GENE	CLASSIFICATION	ZYGOSITY	VARIANT DETECTED	AMINO ACID CHANGE	CANCER RISK
	ATM	<b>LIKELY PATHOGENIC</b>	Het	c.237delA	p.Lys79fsX37	<b>MODERATE</b>

**Variant Summary:** A heterozygous c.237delA (p.Lys79fsX37) likely pathogenic variant was detected in exon 4 of ATM. This frameshift variant is predicted to result in a downstream premature termination codon and has been previously reported in ClinVar and in the literature. Therefore, this variant has been classified as likely to be associated with an increased risk for breast and pancreatic cancer. (NM\_000051; hg19 chr11:g.108099955-108099956)

ATM (ATM serine/threonine kinase; OMIM 607585) is a protein kinase that has roles in normal cell cycle control, development of the nervous and immune systems, and coordination of DNA damage responses promoting genomic stability. Heterozygous germline ATM mutations have been identified and associated with familial breast and pancreatic cancers. Biallelic germline ATM mutations can cause ataxia-telangiectasia, a progressive neurological/immunodeficiency disorder with a predisposition to cancer development, including leukemias and lymphomas.

**Clinical Significance: Moderate Cancer Risk**

This mutation is clinically significant and is associated with an increased cancer risk. Current NCCN guidelines for ATM carriers suggest annual mammography and consideration of breast MRI with contrast starting at age 40. Risk reduction management should be based on family history (www.nccn.org). In addition to this individual being at increased risk, other family members may also be at risk. There is a 50% (1 in 2) chance of a first-degree relative having this mutation. Please call (800) 345-4363 to speak to a Labcorp Genetic Counselor to discuss if targeted analysis for other family members is appropriate.

**This result is associated with the following cancer risks:**

Lifetime Increased Risk	24-48% Female breast
Lifetime Possible Increased Risk	Pancreatic

\*See table below for additional risk information

Date Issued:

**FINAL REPORT**

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sample report 0717

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**RECOMMENDATIONS**

Genetic counseling is recommended to discuss the clinical implications of this result. Genetic counselors are available for health care providers to discuss this result further at (800) 345-GENE. To refer your patient for genetic counseling through Integrated Genetics, please call the scheduling line at (855) 422-2557.

CANCER TYPE	CANCER RISK	RISK FOR GENERAL POPULATION	RELATED TO
<b>Breast</b> To age 70	24-48%	12% Females	ATM
<b>Pancreatic</b> To age 70	Risk not yet determined	1.5%	ATM

**LIST OF ALL GENES IN PANEL**

ATM	MLH1	PTEN	BRCA2	FANCC	RAD51D	FAM175A
NBN	MSH2	TP53	BRIP1	PALB2	STK11	
NF1	MSH6	BARD1	CHEK2	RAD50	MRE11A	
CDH1	PMS2	BRCA1	EPCAM	RAD51C	MUTYH (biallelic)	

**ADDITIONAL INFORMATION**

**Specimen Type:** Whole Blood

**Indication for Testing:** The indication for testing for this patient is a reported personal and/or family history of breast and other cancers.

**Variant Classification:** Variant classification is a weighted assessment that incorporates but is not limited to the following components: prevalence of a variant in the unaffected (general) population, evidence of co-segregation in affected individuals, review of locus specific databases and observed/reported co-occurrence with other deleterious variants within the gene, published functional evidence linking a variant to phenotypes, and predicted functional impact as determined using in-silico analyses. Variants classified within each gene are reported in accordance to the ACMG standards and guidelines. Evidence affecting a variant classification that alters its clinical significance will be reported via an amended report. **Pathogenic variants** negatively affect normal gene function, are associated with disease, and should be used in clinical decision making. **Likely pathogenic variants** are strongly suggestive of normal gene function being negatively affected, and when combined with other evidence of cancer, may be used in clinical decision making. **Variants of uncertain significance (VUS)** have unknown effects on gene function, have not been previously reported or have been reported with inadequate or conflicting evidence regarding pathogenicity, clinical relevance, or cancer risk. A VUS should not be used in clinical decision making but additional monitoring may be considered. **Likely benign variants** are strongly suggestive of having no effect on gene function and are unlikely to have an increased risk for cancer. **Benign variants** have sufficient evidence to be considered of no clinical significance. Likely benign, benign and synonymous variants are not reported, but are available upon request.

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## METHODOLOGY AND LIMITATIONS

Next generation sequencing is used to examine the entire gene coding regions, as well as flanking non-coding regions, of genes known to be involved in the development, progression, and susceptibility of cancer. Flanking regions for the BRCA1 and BRCA2 genes include +/- 20bp and +/-10bp for all other genes. Copy number variations are assessed by microarray or multiple-ligation-probe amplification assay (MLPA) to detect gross deletions and duplications. Due to inherent limitations in the sequence analysis methods used, some variants may be missed. The presence of pseudogenes can interfere with the ability to detect variants in certain genes. Results are reported using nomenclature recommended by the Human Genome Variation Society (HGVS <http://www.hgvs.org/>). Each gene sequence is interpreted independently of all other gene sequences. However, variants in different genes may sometimes interact to cause or modify a typically monogenic disease phenotype. The occurrence of cancer due to genes not analyzed with this test is possible. Additional details regarding technical specifications and limitations of this assay are available on our websites, [www.labcorp.com](http://www.labcorp.com), [www.integratedgenetics.com](http://www.integratedgenetics.com), and [www.integratedoncology.com](http://www.integratedoncology.com).

This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.

## REFERENCES

1. National Comprehensive Cancer Network. Clinical practice guidelines in oncology, genetic/familial high-risk assessment: breast and ovarian. Available at: [www.nccn.org](http://www.nccn.org). 2010. Accessed 5.29.13.
2. Rehm H. et al. Working Group of the American College of Medical Genetics and Genomics Laboratory Quality Assurance Committee. ACMG clinical laboratory standards for next-generation sequencing. *Genet Med*. 2013 Sep;15(9):733-47.
3. Tung N. et al. Frequency of mutations in individuals with breast cancer referred for BRCA1 and BRCA2 testing using next-generation sequencing with a 25-gene panel. *Cancer*. 2015 Jan 121(1):25-33.
4. LaDuca H. et al. Utilization of multigene panels in hereditary cancer predisposition testing. *Genet Med*. 2014 Nov;16(11):830-7.

## Released By:

## PERFORMING LABORATORIES

TG LabCorp RTP 1912 T.W. Alexander Drive, RTP, NC 27709-0150 Lab: (800) 345-4363 Dir: Arundhati Chatterjee, MD  
For inquiries, the physician may contact the lab using the numbers indicated above.