

SAMPLE REPORT, VISTASEQ

Patient Details

DOB: 1/20/1967
Age(y/m/d): 048/02/00
Gender: N
Patient ID: SAMPLE

Specimen Details

Specimen ID: SAMPLE 0030
Date Collected: 6/23/2015
Date Reported: 7/10/2015
Specimen Type: Blood

Client Details

Acct #: CMBP - Test Ac
Ordering Physician: PHY 1, F

POSITIVE

At least one clinically significant variant was detected.

RESULTS AND INTERPRETATION

GENE	CLASSIFICATION	ZYGOSITY	VARIANT DETECTED	AMINO ACID CHANGE	CANCER RISK
+ FAM175A	LIKELY PATHOGENIC	Heterozygous	c.1075A>T	p.Arg359Ter	POSSIBLY ELEVATED

Variant Summary: A heterozygous c.1075A>T likely pathogenic variant was detected in exon 9 of FAM175A. This variant has not been previously reported but is predicted to result in a premature termination codon. A mutation occurring near this variant has been reported to segregate with susceptibility to breast cancer and has been shown to result in loss of normal protein function. Therefore, this variant has been classified as associated with a possibly elevated risk for breast cancer. (NM_139076; hg19 chr4:g.84383777).

FAM175A (Family with sequence similarity 175 or Abraxas; OMIM 611143) encodes a protein that interacts with BRCA1 and is thought to aid normal tumor suppressor functions at sites of DNA damage. Mutations in FAM175A have been identified and associated with a susceptibility to familial breast cancer.

Clinical Significance: Possibly Elevated Cancer Risk

This mutation is clinically significant and is associated with a possibly increased cancer risk. At this time there are no NCCN guidelines for FAM175A mutation carriers. However, modification of surveillance should be based on a patient's personal and/or family history for specific associated cancers and may include initiation of earlier and/or more frequent screening. 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 Possible Increased Risk female breast cancer

* See table below for additional risk information

No additional sequence or copy number variants of clinical significance were detected.

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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
Breast To age 70	risk not yet determined	12%	FAM175A

LIST OF ALL GENES IN PANEL	APC	BRCA1	BRCA2	CDH1	CDKN2A	EPCAM	MLH1
	MSH2	MSH6	PMS2	PTEN	STK11	TP53	MUTYH (biallelic)
	ATM	BMP1A	CDK4	CHEK2	PALB2	SMAD4	FAM175A
	BARD1	BRIP1	RAD51C	NBN	PRKAR1A	RAD51D	

ADDITIONAL INFORMATION

Indication for Testing: The indication for testing for this patient is a reported personal and/or family history of cancers related to Breast Cancer.

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.

METHODOLOGY AND LIMITATIONS

The entire gene coding regions, as well as all flanking noncoding regions, of 27 cancer genes known to be involved in the development and progression of cancers is analyzed by next generation sequencing. 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 gene deletions and duplications. Results are reported using nomenclature recommended by the Human Genome Variation Society (HGVS <http://www.hgvs.org/>).

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METHODOLOGY AND LIMITATIONS (cont)

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. It cannot be excluded that pathogenic variants were missed due to limitations inherent in the sequence analysis method used here. In addition, the presence of a Inherited Cancer Syndrome due to a different genetic cause can also not be ruled out. Any interpretation given here should be clinically correlated with available information about presentation and relevant family history of the patient.

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. 2010. Accessed 5.29.13.
2. American Society of Clinical Oncology Policy Statement Update: Genetic Testing for Cancer Susceptibility. J Clin Oncol. 2003 Jun 15; 21(12):2397-406.
3. 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.

Released By: Director, PhD, Director

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.