Integrated ONCOLOGY LabCorp Specialty Testing Group | Integrated GENETICS LabCorp Specialty Testing Group

VistaSeq℠ Hereditary Cancer Panel

SAMPLE REPORT, VISTASEQ

Patient Details		Specimen Details		Client Details	
DOB:	1/23/1967	**Specimen ID:**	SAMPLE 0070	**Acct #:**	CMBP - Test Ac
Age(y/m/d):	048/05/00	**Date Collected:**	6/23/2015	**Ordering Physician:**	PHY 1, F
Gender:	N	**Date Reported:**	7/14/2015		
Patient ID:	SAMPLE	**Specimen Type:**	Blood		

POSITIVE

At least one clinically significant variant was detected.

RESULTS AND INTERPRETATION

	GENE	CLASSIFICATION	ZYGOSITY	VARIANT DETECTED	AMINO ACID CHANGE	CANCER RISK
+	**MSH2**	**PATHOGENIC**	Heterozygous	c.1147C>T	p.R383Ter	**HIGH**

Variant Summary: A heterozygous c.1147C>T (p.R383Ter) pathogenic variant was detected in exon 7 of MSH2. This nonsense variant has been previously reported once in our database and results in a premature termination codon. This variant has been previously reported in individuals with Lynch syndrome. Therefore, this variant has been classified as associated with an increased risk for a diagnosis of Lynch syndrome associated cancers. (NM_000251; hg19 chr2:g.47656951).

MSH2 (mutS homolog 2; OMIM 609309) encodes an essential component of the DNA mismatch repair system (MMR), repairing errors occuring during DNA replication. Germline mutations in MSH2 have been associated with Lynch syndrome, which is characterized by an increased risk for early-onset colorectal cancer and other tumors including the GI, urological, female reproductive tracts, CNS and skin. Some mutations in MSH2 cause Muir-Torre syndrome, a variant of Lynch syndrome.

Clinical Significance: High Cancer Risk
This mutation is clinically significant and is associated with an increased cancer risk. Current NCCN guidelines emphasize additional screening for MSH2 mutation carriers such as annual/biennial colonoscopy starting at age 20-25 (or 2-5 years prior to the earliest onset of colon cancer reported before age 25 in the family) and discussion of risk reduction surgery such as prophylactic hysterectomy and bilateral salpingo-oophorectomy in women (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 High Risk	40-80% colon, 25-60% endometrial, 4-24% ovarian, 1-14% gastric

*See table below for additional risk information

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

Patient Name: SAMPLE REPORT, VISTASEQ **DOB:** 1/23/1967
Specimen ID: SAMPLE 0070 **Date Collected:** 6/23/2015

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
Colon			
To age 70	40-80%	4.5%	MSH2
Endometrial			
To age 70	25-60%	2.8%	MSH2
Ovarian			
To age 70	4-24%	1.3%	MSH2
Gastric			
To age 70	1-14%	0.9%	MSH2

LIST OF ALL GENES IN PANEL							
	APC	BRCA1	BRCA2	CDH1	CDKN2A	EPCAM	MLH1
	MSH2	MSH6	PMS2	PTEN	STK11	TP53	MUTYH (biallelic)
	ATM	BMPR1A	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 Hereditary Breast and Ovarian Cancer Syndrome.

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/).

Patient Name: SAMPLE REPORT, VISTASEQ **DOB:** 1/23/1967
Specimen ID: SAMPLE 0070 **Date Collected:** 6/23/2015

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 Commitee. 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.