Patient Name	Patient ID	Age	Gender	Order #
SAMPLEREPORT,HCCP	SA00056043	47	M	SA00056043
Ordering Phys CLIENT,CLIENT				**DOB** 06/15/1965
Client Order # SA00056043	**Account Information**			**Report Notes**
Collected 03/21/2013 13:48	C7028846-DLMP Rochester 3050 Superior Drive Rochester, MN 55901			
Printed 04/16/2013 15:00				

Test	Flag	Results	Unit	Reference Value	Perform Site*
Hereditary Colon Cancer Panel			REPORTED 03/26/2013 14:00		
Result Summary		NEGATIVE			MCR
Result Details					MCR

The results for all genes in this panel are negative:
APC, AXIN2, BMPR1A, CDH1, CHEK2, EPCAM, MLH1, MLH3, MSH2, MSH6, MYH, PMS2, PTEN, TP53, SCG5/GREM1, SMAD4, and STK11.

Interpretation MCR

These results reduce the likelihood but do not rule out involvement of the genes evaluated in this panel. We predict that some individuals who have a single-gene associated risk for colon cancer may have a mutation in one of these genes that is not identified by the methods described (e.g. promoter mutations or deep intronic mutations). Additionally, only the common Y165C and G382D mutations associated with MYH-associated polyposis (MAP) were evaluated. These two mutations account for approximately 85% of mutations within the MYH gene in a mixed European Caucasian population. Thus, we predict that approximately 2% of mixed European Caucasian patients will have two unidentified MYH mutations by this method. The percentage of patients with two unidentified mutations may vary in other populations. DNA sequencing of the MYH gene may provide additional diagnostic information.

Importantly, the clinical phenotype that is observed in this patient and/or family may be due to disease-causing mutations in other genes associated with hereditary colon cancer.

Due to the limitations of Next Generation Sequencing, small deletions and insertions greater than 8 nucleotides in length will not be detected by this test. If a diagnosis of one of the syndromes on this panel is still suspected, consider full gene sequencing using traditional Sanger methods.

A genetic consultation may be of benefit.

Caution MCR

CLINICAL CORRELATIONS
Test results should be interpreted in context of clinical findings, family history, and other laboratory data. Misinterpretation of results may occur if the information provided is inaccurate or incomplete.

Performing Site Legend on Last Page of Report

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If testing was performed because of a family history colon cancer or colon polyps, it is often useful to first test an affected family member. Identification of a specific gene mutation in this family would lead to more direct testing of at risk individuals.

TECHNICAL LIMITATIONS
Due to the limitations of Next Generation Sequencing, small deletions and insertions greater than 8 nucleotides in length will not be detected by this test. If a diagnosis of one of the syndromes on this panel is still suspected, consider full gene sequencing using traditional Sanger methods.

Rare polymorphisms exist that could lead to false negative or positive results. If results obtained do not match the clinical findings, additional testing should be considered.

Bone marrow transplants from allogenic donors will interfere with testing. Call Mayo Medical Laboratories for instructions for testing patients who have received a bone marrow transplant.

EVALUATION TOOLS
Multiple in-silico evaluation tools were used to assist in the interpretation of these results. These tools are updated regularly, therefore changes to these algorithms may result in different predictions for a given alteration. Additionally, the predictability of these tools for the determination of pathogenicity is currently unvalidated.

Unless reported or predicted to cause disease, alterations found deep in the intron or alterations that do not result in an amino acid substitution are not reported.

RECLASSIFICATION OF VARIANTS - POLICY
All detected alterations are evaluated according to ACMG recommendations (Genet Med 2008:10(4):294-300). Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance. At this time, it is not standard practice for the laboratory to systematically review LIKELY DELETERIOUS alterations or VARIANTS OF UNCERTAIN SIGNIFICANCE that are detected and

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reported. The laboratory encourages health care providers to contact the laboratory at any time to learn how the status of a particular variant may have changed over time.

TEST CLASSIFICATION
Laboratory developed test.

Reason For Referral MCR

Test for the presence of mutations in the genes included in the Hereditary Colon Cancer Panel.

Method MCR

Next generation sequencing and/or Sanger sequencing was performed to test for the presence of a mutation in all coding regions and intron/exon boundaries of the APC, AXIN2, BMPR1A, CDH1, CHEK2, MLH1, MLH3, MSH2, MSH6, TP53, PTEN (including analysis of the promoter: c.-1250_c.1), SMAD4, and STK11 genes. Additionally, array comparative genomic hybridization (aCGH) was used to test for the presence of large deletions and duplications in the APC, AXIN2, BMPR1A, CDH1, CHEK2, EPCAM, MLH1, MLH3, MSH2, MSH6, TP53, PTEN, SMAD4, SCG5/GREM1, and STK11. Next generation sequencing was performed to test for the p.Y165C and p.G382D mutations in the MYH (MutYH) gene.

Bi-directional sequence analysis with long range PCR was performed to test for the presence of a mutation in all coding regions and intron/exon boundaries of the PMS2 gene. Gene dosage analysis by multiplex ligation-dependent probe amplification (MLPA) was used to test for the presence of large deletions and duplications in the PMS2 gene.

All reported alterations detected by next generation sequencing were confirmed using Sanger sequencing or other PCR-based assay.

Mutation nomenclature is based on GenBank accession numbers listed below.

GENE	GENBANK#
APC	NM 000038.5
AXIN2	NM 004655.3
BMPR1A	NM 004329.2
CDH1	NM 004360.3
CHEK2	NM 007194.3

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Test		Flag	Results	Unit	Reference Value	Perform Site*
EPCAM	NM 002354.2					
MLH1	NM 000249.3					
MLH3	NM 001040108.1					
MSH2	NM 000251.1					
MSH6	NM 000179.2					
MYH/MutYH	NM 001048171.1					
TP53	NM 000546.4					
PMS2	NM 000535.5					
PTEN	NM 000314.4					
SCG5/GREM1	NM 001144757.1					
SMAD4	NM 005359.5					
STK11	NM 000455.4					
Specimen			Blood			MCR
Reviewed By						MCR
Matthew John Ferber PhD						
Release Date			26 Mar 2013 13:59			MCR

* Performing Site:

MCR	Mayo Clinic Laboratories - Rochester Main Campus 200 First St SW Rochester, MN 55905	Lab Director: Franklin R. Cockerill, III, M.D.