



## **Hereditary Colon Cancer Multi-Gene Panel**

Test ID: HCCP

### **USEFUL FOR:**

- Tests for mutations in the following genes associated with hereditary colon cancer: APC, AXIN2, BMPR1A, CDH1, CHEK2, EPCAM, MLH1, MLH3, MSH2, MSH6, MYH (MUTYH), TP53, PMS2, PTEN, SCG5-GREM1, SMAD4, and STK11
- Providing a comprehensive evaluation for hereditary colon cancer in patients with a personal or family history suggestive of a hereditary colon cancer syndrome
- Serving as a second-tier test for patients in which previous targeted gene mutation analyses for specific hereditary colorectal cancer-related genes was negative
- Establishing a diagnosis of a hereditary colon cancer syndrome in some cases, allowing for targeted cancer surveillance of associated extra-colonic organs known to be at increased risk for cancer
- Identifying mutations within genes known to be associated with increased risk for colon cancer allowing for predictive testing of at-risk family members

**METHODOLOGY:** Custom Sequence Capture and Targeted Next Generation Sequencing followed by Polymerase Chain Reaction (PCR), Sanger Sequencing and Gene Dosage Analysis by Array Comparative Genomic Hybridization (aCGH) or Multiplex Ligation-Dependent Probe Amplification (MLPA)

**REFERENCE VALUES:** An interpretive report will be provided.

**SPECIMEN REQUIREMENTS:** Specimen must arrive within 96 hours of collection.

**Specimen Type:** Whole blood

**Container/Tube:**

**Preferred:** Lavender top (EDTA) or yellow top (ACD)

**Acceptable:** Any anticoagulant

**Specimen Volume:** 10 mL

**Collection Instructions:**

1. Invert several times to mix blood.
2. Send specimen in original tube.

**Additional Information:** To ensure minimum volume and concentration of DNA is met, the preferred volume of blood must be submitted. Testing may be canceled if DNA requirements are inadequate

### **NOTE:**

- New York Clients-Informed consent is required. Please document on the request form or electronic order that a copy is on file. An Informed Consent for Genetic Testing (Supply T576) is available in Special Instructions.

- Molecular Genetics-Colon Cancer Patient Information Sheet (Supply T521) in Special Instructions

**SPECIMEN STABILITY INFORMATION:**

Specimen Type	Temperature	Time
Varies	Ambient (preferred)	
	Frozen	
	Refrigerated	

**CAUTIONS:**

**Clinical Correlations:**

- A small percentage of individuals who have involvement of 1 or more of the genes on the panel may have a mutation that is not identified by the methods performed (eg, promoter mutations, deep intronic mutations). The absence of a mutation, therefore, does not eliminate the possibility of a hereditary colorectal cancer syndrome or other heritable risk for colon cancer. For predictive testing of asymptomatic individuals, it is important to first document the presence of a gene mutation in an affected family member.
- 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.

**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 these syndromes on this panel is still suspected, consider full gene sequencing using traditional Sanger methods.
- In some cases, DNA variants of undetermined significance may be identified.
- Rare polymorphisms exist that could lead to false-negative or false-positive results. If results obtained do not match the clinical findings, additional testing should be considered.
- In addition to disease-related probes, the multiplex ligation-dependent probe amplification technique utilizes probes localized to other chromosomal regions as internal controls. In certain circumstances, these control probes may detect other diseases or conditions for which this test was not specifically intended. Results of the control probes are not normally reported. However, in cases where clinically relevant information is identified, the ordering physician will be informed of the result and provided with recommendations for any appropriate follow-up testing.
- A previous bone marrow transplant from an allogenic donor will interfere with testing. Call Mayo Medical Laboratories at 800-533-1710 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. These and common polymorphisms identified for this patient are available upon request.

Reclassification of Variants-Policy:

- All detected alterations are evaluated according to American College of Medical Genetics and Genomics recommendations. 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 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.

**CPT CODE:**

81201-APC (adenomatous polyposis coli) (eg, familial adenomatosis polyposis [FAP], attenuated FAP) gene analysis; full gene sequence  
81228-Cytogenomic constitutional (genome-wide) microarray analysis; interrogation of genomic regions for copy number variants (eg, Bacterial Artificial Chromosome [BAC] or oligo-based comparative genomic hybridization [CGH] microarray analysis)  
81292-MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis  
81295-MSH2 (mutS homolog2, colon cancer, nonpolyposis type 1) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis  
81298-MSH6 (mutS homolog 6[E.coli])(eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis  
81317-PMS2 (postmeiotic segregation increased 2 [S. cerevisiae])(eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis  
81319- PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants  
81321-PTEN (phosphatase and tensin homolog) (eg, Cowden syndrome, PTEN hamartoma tumor syndrome) gene analysis; full gene analysis  
81401-MUTYH (mutY homolog [E. coli]) (eg, MYH-associated polyposis), common variants (eg, Y165C, G382D)  
81405-P53 (tumor protein 53) (eg, Li-Fraumeni syndrome, tumor samples), full gene sequence or targeted sequence analysis of >5 exons  
81406-CDH1 (cadherin 1, type 1, E-cadherin [epithelial]) (eg, hereditary diffuse gastric cancer), full gene analysis  
81479-Unlisted molecular pathology code

**DAY(S) SET UP:** Every other Wednesday, 10 a.m.    **ANALYTIC TIME:** 6 weeks

QUESTIONS: Contact your Mayo Medical Laboratories' Regional Manager or  
Marvin H. Anderson, Jr., MML Laboratory Technologist Resource Coordinator  
Telephone: 800-533-1710