High Risk Colorectal Cancer: Sequencing Panel

**Test Code:** MM205  
**Turnaround time:** 4 weeks  
**CPT Codes:** 81435 x1

### Condition Description

Emory Genetics Laboratory (EGL) High Risk Colorectal Cancer Panel include the well-described hereditary cancer predisposition syndromes; Lynch syndrome, familial adenomatous polyposis, and MYH-associated polyposis. Lynch syndrome, familial adenomatous polyposis, and MutY homolog (MUTYH)-associated polyposis are three major known types of inherited colorectal cancer, which accounts for up to 5% of all colon cancer cases. Lynch syndrome is most frequently caused by mutations in the mismatch repair genes **MLH1, MSH2, MSH6, PMS2, and EPCAM**, and is inherited in an autosomal dominant manner.

Familial adenomatous polyposis is manifested as colonic polyposis caused by mutations in the **APC** gene and is also inherited in an autosomal dominant manner. Finally, MYH-associated polyposis is caused by mutations in the **MUTYH** gene and is inherited in an autosomal recessive manner but may or may not be associated with polyps. There are variants of both familial adenomatous polyposis (Gardner syndrome—with extracolonic features—and Turcot syndrome, which features medulloblastoma) and Lynch syndrome (Muir-Torre syndrome features sebaceous skin carcinomas, and Turcot syndrome features glioblastomas). Although a clinical diagnosis of familial adenomatous polyposis can be made using colonoscopy, genetic testing is needed to inform at-risk relatives. Because of the overlapping phenotypes between attenuated familial adenomatous polyposis, MYH-associated polyposis, and Lynch syndrome, genetic testing is needed to distinguish among these conditions. This distinction is important, especially for women with Lynch syndrome, who are at increased risk for gynecological cancers.

Reference:

### Genes

**APC, ATM, BLM, BMPR1A, CDH1, CHEK2, MLH1, MSH2, MSH6, MUTYH, PMS2, PTEN, SMAD4, STK11, TP53**

### Indications

The test is indicated for:

- Individuals with a clinical or suspected diagnosis of high risk colorectal cancer.

### Methodology

**Next Generation Sequencing:** In-solution hybridization of all coding exons is performed on the patient's genomic DNA. Although some deep intronic regions may also be analyzed, this assay is not meant to interrogate most promoter regions, deep intronic regions, or other regulatory elements, and does not detect single or multi-exon deletions or duplications. Direct sequencing of the captured regions is performed using next generation sequencing. The patient's gene sequences are then compared to a standard reference sequence. Potentially causative variants and areas of low coverage are Sanger-sequenced. Sequence variations are classified as pathogenic, likely pathogenic, benign, likely benign, or variants of unknown significance. Variants of unknown significance may require further studies of the patient and/or family members.

### Detection

**Next Generation Sequencing:** Clinical Sensitivity: Unknown. Mutations in the promoter region, some mutations in the introns and other regulatory element mutations cannot be detected by this analysis. Large deletions/duplications will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's clinical/biochemical phenotype.

Analytical Sensitivity: ~99%.

### Specimen Requirements

Submit only 1 of the following specimen types

**Type: Whole Blood**

Specimen Requirements:

In EDTA (purple top) tube:
- Infants (2 years): 3-5 ml
- Older Children & Adults: 5-10 ml

Specimen Collection and Shipping: Ship sample at room temperature with overnight delivery.
Type: Isolated DNA

Specimen Requirements:

In microtainer: 60 ug

Isolation using the Qiagen™ Puregene kit for DNA extraction is recommended.

Specimen Collection and Shipping: Refrigerate until time of shipment in 100 ng/ul of TE buffer. Ship sample at room temperature with overnight delivery.

Special Instructions

This test is for germline mutation analysis. DNA isolated from FFPE tumor samples is not suitable for this test.

Related Tests

- Hereditary Cancer Syndrome: Sequencing Panel.
- High Risk Colorectal Cancer: Deletion/Duplication Panel.