**Overview**

**Useful For**
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 whom previous targeted gene mutation analyses for specific hereditary colorectal cancer-related genes were 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

**Genetics Test Information**
This test includes next-generation sequencing, Sanger sequencing, array comparative genomic hybridization, and multiplex ligation-dependent probe amplification to evaluate for the genes listed on the panel.

Prior Authorization is available for this assay; see Special Instructions

See [Targeted Gene Regions Interrogated by Hereditary Colon Cancer Panel](#) in Special Instructions for details regarding the targeted gene regions identified by this test.

**Testing Algorithm**
The following algorithms are available in Special Instructions:

- Lynch Syndrome Testing Algorithm
- Colonic Polyposis Syndromes Testing Algorithm

**Special Instructions**
- Molecular Genetics: Inherited Cancer Syndromes Patient Information
- Informed Consent for Genetic Testing
- Colonic Polyposis Syndromes Testing Algorithm
- Hereditary Colon Cancer Multi-Gene Panel Prior Authorization Ordering Instructions
- Targeted Genes Interrogated by Hereditary Colon Cancer Panel
- Lynch Syndrome Testing Algorithm
- Informed Consent for Genetic Testing (Spanish)

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

**NY State Available**
Yes

**Specimen**
**Specimen Type**
Varies

**Shipping Instructions**
Specimen preferred to arrive within 96 hours of collection.

**Specimen Required**

**Patient Preparation:** A previous bone marrow transplant from an allogenic donor will interfere with testing. Call 800-533-1710 for instructions for testing patients who have received a bone marrow transplant.

**Specimen Type:** Whole blood

**Container/Tube:**

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

**Acceptable:** Any anticoagulant

**Specimen Volume:** 3 mL

**Collection Instructions:**
1. Invert several times to mix blood.
2. Send specimen in original tube.

**Additional Information:**
1. 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.

2. **Prior Authorization** is available for this test. Submit the required form with the specimen.

**Forms**
1. **New York Clients-Informed consent is required.** Document on the request form or electronic order that a copy is on file. The following documents are available in Special Instructions:
   - [Informed Consent for Genetic Testing](T576)
   - [Informed Consent for Genetic Testing-Spanish](T826)

2. [Molecular Genetics: Inherited Cancer Syndromes Patient Information](T519) in Special Instructions

3. [Hereditary Colon Cancer Multi-Gene Panel Prior Authorization Ordering Instructions](T729) in Special Instructions

4. If not ordering electronically, complete, print, and send an [Oncology Test Request](T729) (T729) with the specimen.

**Specimen Minimum Volume**
1 mL

**Reject Due To**
All specimens will be evaluated by Mayo Clinic Laboratories for test suitability.

**Specimen Stability Information**

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
<th>Special Container</th>
</tr>
</thead>
<tbody>
<tr>
<td>Varies</td>
<td>Ambient (preferred)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Frozen</td>
<td></td>
<td></td>
</tr>
<tr>
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**Clinical and Interpretive**

**Clinical Information**

Colorectal cancer occurs in approximately 5% to 6% of individuals in the general population. In rare cases, individuals with a family history of colorectal cancer may be at increased risk for colon and other cancers due to a single-gene predisposition syndrome, known as hereditary colorectal cancer. The 2 most common hereditary colorectal cancer syndromes are Lynch syndrome and familial adenomatous polyposis (FAP). However, there are multiple other genes that are also known to cause to hereditary colorectal cancer or contribute to an increased risk for colorectal cancer. This panel uses next-generation sequencing (NGS), array comparative genomic hybridization (aCGH), and other technologies to evaluate for germline mutations in 17 genes known to be associated with an increased risk for colon cancer development. Two of the genes listed, *CHEK2* and *MLH3*, are not associated with a known hereditary cancer syndrome defined by a distinct spectrum of tumors. However, literature suggests that mutations in these genes may confer an increased risk for colon cancer and, therefore, are predicted to contribute to cancer risk in patients and families.

<table>
<thead>
<tr>
<th>Gene</th>
<th>Known Association</th>
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<tbody>
<tr>
<td>MLH1</td>
<td>Lynch syndrome</td>
</tr>
<tr>
<td>MSH2</td>
<td>Lynch syndrome</td>
</tr>
<tr>
<td>MSH6</td>
<td>Lynch syndrome</td>
</tr>
<tr>
<td>PMS2</td>
<td>Lynch syndrome</td>
</tr>
<tr>
<td>EPCAM</td>
<td>Lynch syndrome</td>
</tr>
<tr>
<td>APC</td>
<td>Familial adenomatous polyposis</td>
</tr>
<tr>
<td>MYH/MutYH</td>
<td><em>MYH</em>-associated polyposis</td>
</tr>
<tr>
<td>SCG5/GREM1</td>
<td>Hereditary mixed polyposis syndrome</td>
</tr>
<tr>
<td>STK11</td>
<td>Peutz-Jeghers syndrome</td>
</tr>
<tr>
<td>SMAD4</td>
<td>Juvenile polyposis syndrome</td>
</tr>
<tr>
<td>BMPR1A</td>
<td>Juvenile polyposis syndrome</td>
</tr>
<tr>
<td>PTEN</td>
<td><em>PTEN</em> hamartoma tumor syndrome (ie, Cowden syndrome)</td>
</tr>
<tr>
<td>CDH1</td>
<td>Hereditary diffuse gastric cancer</td>
</tr>
<tr>
<td>AXIN2</td>
<td>Oligodontia-colorectal cancer syndrome</td>
</tr>
<tr>
<td>TP53</td>
<td>Li-Fraumeni syndrome</td>
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</table>
Test Definition: HCRC
Hereditary Colon Cancer Panel

<table>
<thead>
<tr>
<th>Gene</th>
<th>Classification</th>
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<tbody>
<tr>
<td>CHEK2</td>
<td>Low-risk gene</td>
</tr>
<tr>
<td>MLH3</td>
<td>Low-risk gene</td>
</tr>
</tbody>
</table>

Indications for testing include but are not limited to:

- Patients in whom no specific colorectal cancer syndrome is evident but for whom there is a clear familial component

- Patients whose family history is consistent with familial colorectal cancer type X(1)

- Patients with a strong suspicion for a single-gene hereditary colon cancer syndrome based on an autosomal dominant pattern of colon cancer in the family

- Patients with a personal or family history of colonic polyposis

Reference Values
An interpretive report will be provided.

Interpretation
All detected alterations are evaluated according to American College of Medical Genetics and Genomics recommendations.(2) Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance.

Cautions
Clinical Correlations:
Some 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:
In some cases, DNA variants of undetermined significance may be identified.

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. Single or multiexon deletions as well as whole gene deletions will be detected by array comparative genomic hybridization (aCGH).

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.

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 not validated.

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.

Clinical Reference


Performance
**Method Description**


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

**PDF Report**

No

**Day(s) and Time(s) Test Performed**

Performed weekly, varies

**Analytic Time**

4 weeks

**Maximum Laboratory Time**

5 weeks

**Specimen Retention Time**

Whole Blood: 2 weeks (if available) Extracted DNA: Indefinitely

**Performing Laboratory Location**

Rochester

**Fees and Codes**

**Fees**

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact Customer Service.

**Test Classification**

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with...
Test Definition: HCRC
Hereditary Colon Cancer Panel

CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information

81435

81436

LOINC® Information

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<th>Test Order Name</th>
<th>Order LOINC Value</th>
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<tbody>
<tr>
<td>HCRC</td>
<td>Hereditary Colon Cancer Panel</td>
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<td>Released By</td>
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Prior Authorization

Insurance preauthorization is available for this testing; forms are available in Special Instructions.

Patient financial assistance may be available to those who qualify. Patients who receive a bill from Mayo Clinic Laboratories will receive information on eligibility and how to apply.