

## Using Genetic Testing to Assess Risk of Hereditary Non-polyposis Colon Cancer (HNPCC)

### Indications:

- Amsterdam II criteria met
- Modified Bethesda guidelines met and high MSI demonstrated for tumor tissue
- High MSI demonstrated for tumor tissue and/or MMR-gene product absent based on immunohistochemical analysis of tumor tissue
- Known familial mutations in MMR gene

### Benefits:

Genetic testing for HNPCC can:

- Confirm a suspected clinical diagnosis of HNPCC and alert patients to risk of additional HNPCC-associated tumors, guiding extent of surgery and ongoing cancer surveillance
- Identify the familial mutation(s) and allow family testing to
  - detect presymptomatic mutation carriers among family members of patients, enabling timely initiation of colonoscopy and other preventative measures
  - identify family members who do not carry the familial mutation and are therefore not at greatly increased risk of HNPCC-associated cancers
- Inform genetic counseling

### Background:

- HNPCC (Lynch syndrome) is an autosomal dominant familial cancer syndrome estimated to account for 1-3% of colorectal cancer and, in women, 1-2% of endometrial cancer.<sup>1,2</sup>
- HNPCC has been associated with mutations in the genes *MLH1*, *MSH2*, *MSH6*, and *PMS2*. Mutation carriers have a 50-80% lifetime risk of colon cancer, a 40-60% lifetime risk of endometrial cancer (in females), and increased risk of several other cancers.<sup>1,2</sup>
- HNPCC-associated cancers often show unusually early age of onset, synchronicity, and increased recurrence risk.<sup>1,2</sup>
- In mutation carriers, regular screening by colonoscopy and timely treatment by colectomy has been shown to reduce colon cancer incidence and death from colon cancer.<sup>2</sup>
- Once the specific mutation causing HNPCC in a particular family has been identified, genetic testing can help to detect both carriers and non-carriers among family members with close to 100% accuracy.<sup>3</sup>
- Sequencing of the coding regions of *MLH1*, *MSH2*, *MSH6*, and *PMS2* is estimated to detect about 65-90% of HNPCC-associated mutations.<sup>1</sup>

**References:** 1. Kohlmann W, Gruber, SB. (2006) GeneReviews.

<http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gene&part=hnpsc>. Accessed 072810.

2. Jasperson KW, et al (2010) *Gastroenterology* 138:2044-58. 3. Winawer S, et al (2003) *Gastroenterology* 124:544-60.

**Ordering Information:** Please see other side.

## Ordering Information for Hereditary Non-polyposis Colon Cancer (HNPCC) Testing

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### Ordering Information for Single Gene Tests

Gene(s)	Test Code
<i>MLH1</i>	252830
<i>MSH2</i>	252837
<i>MSH6</i>	252853
<i>PMS2</i>	252847

### Ordering Information for Multi-Gene Panels\*

<i>MLH1, MSH2</i>	252844
<i>MLH1, MSH2, MSH6</i>	252860
<i>MLH1, MSH2, MSH6, PMS2</i>	252863

### Family Testing (single amplicon)

Family Testing is available for both genes. Please contact Client Services at 1-866-647-0735 for requirements.

### Test Methodology

- Amplification by polymerase chain reaction (PCR); sequencing of entire protein-coding region

NOTE: Specimens must be accompanied by a completed consent form. In the case of family tests (ie, known mutations), a copy of the result of the first patient tested in the family (the index case) must be submitted unless that test was performed at Correlagen. Other family members are subsequently tested for the specific mutation found in the first patient tested.

**For test information, sample requirements, or to request a sample shipping kit,  
please contact Client Services at 1-866-647-0735 or visit us on the web at  
[www.correlagen.com](http://www.correlagen.com).**