HNPCC/Lynch Syndrome (MSH2) Sequencing and Deletion/Duplication

Reference Interval:

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<td>MSH2 Full Gene Sequencing</td>
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<td>MSH2 Deletion/Duplication/ Inversion</td>
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Interpretive Data:

Background Information for HNPCC/Lynch syndrome (MSH2) Sequencing and Deletion/Duplication:

Characteristics of Lynch syndrome: Increased risk of colorectal and extra-colonic cancers including endometrial, renal, ureter, ovary, stomach, small intestine, and hepatobiliary tract.

Incidence: 1-2 percent of colorectal cancer is due to pathogenic mismatch repair gene variants.

Inheritance: Autosomal dominant.

Penetrance: 80 percent lifetime risk of colorectal cancer; 20-60 percent risk for endometrial cancer.

Cause: Pathogenic germline MLH1, MSH2, MSH6, and PMS2 gene variants.

Gene tested: MSH2

Clinical Sensitivity: 40 percent of Lynch syndrome is due to pathogenic MSH2 variants.

Methodology: Bidirectional sequencing of MSH2 coding regions and intron-exon boundaries; multiplex ligation-dependent probe amplification (MLPA) to detect large exonic deletions and duplications of MSH2, EPCAM (TACSTD1) exon 9 and the 10Mb MSH2 exons1-7 inversion.

Analytical Sensitivity & Specificity: 99 percent.

Test Limitations: Diagnostic errors can occur due to rare sequence variations. The breakpoints of large deletions/duplications/inversions will not be determined. Deep intronic and regulatory region variants will not be detected. Variants in genes other than MSH2 and TACSTD1, as described above, will not be detected.

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