0051654 HNPCC/Lynch Syndrome (*MSH2)* Sequencing and Deletion/Duplication MSH2 FGA

Reference Interval:

Test Number	Components	Reference Interval
	MSH2 Full Gene Sequencing	By report
	MSH2 Deletion/Duplication/ Inversion	By report

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, pelvis, 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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