**Lynch Syndrome (HNPCC) Testing**

All colorectal cancer and endometrial tumors

Screen for mismatch repair deficiency

ORDER
Mismatch Repair by Immunohistochemistry

<sup>a</sup> Abnormal per IHC

High clinical suspicion of Lynch syndrome

ORDER
Microsatellite Instability (MSI) HNPCC/Lynch Syndrome by PCR

Instability in at least 2 of 5 microsatellite markers

Instability in 1 microsatellite marker

No instability present

High

Low

Stable

Variant present

Variant absent (wild type)

Consider germline testing of mismatch repair genes

ORDER
Lynch Syndrome Panel, Sequencing and Deletion/Duplication

Lynch syndrome unlikely

Probable sporadic colorectal cancer

Consider germline pathogenic variants in MSH2 and MSH6

Associated with germline pathogenic variants in MSH2 or, more rarely, in MSH6

CONSIDER
Lynch Syndrome Panel, Sequencing and Deletion/Duplication

Single gene testing

(Additional testing)

Lynch syndrome unlikely

Abnormal per IHC

Abnormal staining for MLH1 and PMS2

Test for BRAF V600E variant

ORDER
BRAF Codon 600 Mutation Detection with Reflex to MLH1 Promoter Methylation

Associated with germline pathogenic variants in MSH2 or, more rarely, in MSH6

CONSIDER
Lynch Syndrome Panel, Sequencing and Deletion/Duplication

Single gene testing

(Additional testing)

Abnormal staining for MSH2 and MSH6

Associated with germline pathogenic variants in MSH6

CONSIDER
Lynch Syndrome Panel, Sequencing and Deletion/Duplication

Single gene testing

(Additional testing)

Abnormal staining for MSH6

Associated with germline pathogenic variants in PMS2 or, more rarely, in MLH1

CONSIDER
Lynch Syndrome Panel, Sequencing and Deletion/Duplication

Single gene testing

(Additional testing)

Abnormal staining for PMS2

Abnormal staining for MSH2 and MSH6

Abnormal staining for PMS2

**Abbreviations**

HNPCC Hereditary nonpolyposis colorectal cancer

IHC Immunohistochemistry

PCR Polymerase chain reaction

<sup>a</sup> Loss of MLH1 may be due to either acquired hypermethylation (in sporadic tumors) or a germline mutation (in Lynch syndrome).

<sup>b</sup> Panel (reflex) tests are available (Mismatch Repair by Immunohistochemistry with Reflex to BRAF Codon 600 Mutation and MLH1 Promoter Methylation; Mismatch Repair by Immunohistochemistry with Reflex to MLH1 Promoter Methylation).

<sup>c</sup> Not applicable to endometrial cancers; order only MLH1 Promoter Methylation.

<sup>d</sup> Targeted testing for a variant previously identified in a family member is available (Familial Targeted Sequencing).

<sup>e</sup> Single gene testing is not available at ARUP Laboratories.