Specimen Collected: 15-Sep-21 08:34

Mismatch Repair IHC with Reflex to MLH1 | **Received: 15-Sep-21 09:44** **Report/Verified: 15-Sep-21 09:46**

Procedure	Result	Units	Reference Interval
Mismatch Repair by IHC Result	Normal [t1 i1]		
Mismatch Repair by IHC with MLH1	Abnormal		
Mismatch Repair by IHC with MSH2	Abnormal		
Mismatch Repair by IHC with MSH6	Abnormal		
Mismatch Repair by IHC with PMS2	Normal		
Client Case or Ref #	1		
MSI Tissue Source	2		

MLH1 Methylation PCR | **Received: 15-Sep-21 09:44** **Report/Verified: 15-Sep-21 09:48**

Procedure	Result	Units	Reference Interval
MLH1 Promoter Methylation	Not Detected [i2]		
Block ID	4		

Interpretive Text

t1: 15-Sep-21 08:34 (Mismatch Repair by IHC Result)

Normal immunohistochemical staining for mismatch repair proteins correlates well with the absence of microsatellite instability by PCR. Since the correlation is not perfect, however, a direct evaluation by PCR may be helpful to exclude the possibility of microsatellite instability (refer to Microsatellite Instability/HNPCC 0051740). Also, the lack of microsatellite instability in an adenoma is not as reliable a criterion for excluding Lynch syndrome (HNPCC) as the lack of instability in a cancer. Controls worked appropriately.

This result has been reviewed and approved by Joshua F. Coleman, M.D.

Test Information

i1: Mismatch Repair by IHC Result

INTERPRETIVE INFORMATION: Mismatch Repair IHC with Reflex to MLH1

Immunohistochemical staining for mismatch repair proteins can be used as a surrogate test for microsatellite instability as measured by PCR. Normal results correlate well with the absence of microsatellite instability, while abnormal results correlate well with the presence of microsatellite instability. Abnormal results may also qualify patients for immune checkpoint inhibitor treatment. The immunohistochemical staining pattern can also be used as a guide for the subsequent germline evaluation of mismatch repair genes (refer to Lynch Syndrome - HNPCC) testing algorithm at ARUPconsult.com). Normal staining results consist of any level

Test Information

i1: Mismatch Repair by IHC Result

of staining in the tumor cells (unless evidence of clonal loss). Abnormal staining results consist of complete loss of staining in the tumor cells, in the presence of retained staining in normal (non-tumor) cells, which serve as an internal control. An abnormal overall result may qualify patients for immune checkpoint inhibitor treatment, in the appropriate clinical setting.

Genetic counseling is recommended for the interpretation of all results.

Assay is performed on formalin fixed paraffin-embedded tissue. Antibody clone for MLH1 is ES05, MSH2 is FE11, MSH6 is EP49, and PMS2 is EP51. Detection system is a proprietary polymeric HRP.

This test was developed and its performance characteristics determined by ARUP Laboratories. It has not been cleared or approved by the US Food and Drug Administration. This test was performed in a CLIA certified laboratory and is intended for clinical purposes.

i2: MLH1 Promoter Methylation

TEST INFORMATION: MLH1 Promoter Methylation, Paraffin

MLH1 methylation is common in sporadic microsatellite unstable tumors, like colorectal cancer and endometrial cancer, and rarely occurs in Lynch syndrome (hereditary non-polyposis colon cancer or HNPCC). Therefore, the presence of MLH1 methylation suggests that the tumor is sporadic and not associated with Lynch syndrome. However, since there have been rare reports of Lynch syndrome-associated MLH1 methylation, all results should be interpreted within the clinical context. The lack of MLH1 methylation in a mismatch repair deficient tumor suggests that it may be associated with Lynch syndrome, and germline evaluation is suggested. Finally, low level MLH1 methylation is not reported as positive, since it does not correlate with MLH1 inactivation and microsatellite instability.

METHODOLOGY: DNA is isolated from tumor tissue microdissected from prepared slides. DNA is treated with sodium bisulfite, followed by amplification of a segment of the MLH1 promoter region using methylation specific real-time PCR. The MLH1 methylation level is calculated by comparison to the amplification of a reference gene.

LIMITATIONS: Methylation at locations other than those covered by the primers and probes will not be detected. Results of this test must always be interpreted within the clinical context and other relevant data, and should not be used alone for a diagnosis of malignancy. This test is not intended to detect minimal residual disease.

ANALYTICAL SENSITIVITY: Methylation levels below 10 percent are reported as negative.

Test Information

i2: MLH1 Promoter Methylation

This test was developed and its performance characteristics determined by ARUP Laboratories. It has not been cleared or approved by the US Food and Drug Administration. This test was performed in a CLIA certified laboratory and is intended for clinical purposes.