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*****Example Report*****

Patient Age/Gender: 67 years Female
Printed: 26-Jun-20 15:07:04

Procedure	Result	Units	Ref Interval	Accession	Collected	Received	Reported/ Verified
MLH1 Promoter Methylation	**Positive *f**			20-178-900045	26-Jun-20 10:41:00	26-Jun-20 10:44:00	26-Jun-20 14:54:01
Block ID	0			20-178-900045	26-Jun-20 10:41:00	26-Jun-20 10:44:00	26-Jun-20 14:54:01
Mismatch Repair by IHC Result	Abnormal			20-178-900045	26-Jun-20 10:41:00	26-Jun-20 10:44:00	26-Jun-20 11:25:35
Mismatch Repair by IHC with MLH1	Abnormal			20-178-900045	26-Jun-20 10:41:00	26-Jun-20 10:44:00	26-Jun-20 11:25:35
Mismatch Repair by IHC with MSH2	Normal			20-178-900045	26-Jun-20 10:41:00	26-Jun-20 10:44:00	26-Jun-20 11:25:35
Mismatch Repair by IHC with MSH6	Normal			20-178-900045	26-Jun-20 10:41:00	26-Jun-20 10:44:00	26-Jun-20 11:25:35
Mismatch Repair by IHC with PMS2	Abnormal			20-178-900045	26-Jun-20 10:41:00	26-Jun-20 10:44:00	26-Jun-20 11:25:35
Client Case or Ref #	SF20-14587 C2			20-178-900045	26-Jun-20 10:41:00	26-Jun-20 10:44:00	26-Jun-20 11:25:35
MSI Tissue Source	Colon			20-178-900045	26-Jun-20 10:41:00	26-Jun-20 10:44:00	26-Jun-20 11:25:35

26-Jun-20 10:41:00 Mismatch Repair by IHC Result
Abnormal immunohistochemical staining for mismatch repair proteins correlates well with the presence of microsatellite instability by PCR. The BRAF codon 600 mutation test (0051750) may be helpful in distinguishing sporadic from Lynch (HNPCC) associated colorectal cancers with abnormal MLH1 immunostaining. Controls worked appropriately.

This result has been reviewed and approved by Allie Grossmann, M.D., Ph.D.

26-Jun-20 10:41:00 MLH1PCR:

The tumor tested was identified and selected by a Board Certified AP/CP Pathologist.
26-Jun-20 10:41:00 MLH1 Promoter Methylation:

MLH1 promoter methylation was detected.

This result has been reviewed and approved by Anna Matynia, M.D.

26-Jun-20 10:41:00 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 developed and characteristics determined by ARUP Laboratories. See Compliance Statement B: aruplab.com/CS

26-Jun-20 10:41:00 Mismatch Repair by IHC Result:
INTERPRETIVE INFORMATION: Mismatch Repair by
Immunohistochemistry with Reflex
to MLH1 Promoter Methylation
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. 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).

Genetic counseling is recommended for the interpretation of all results.

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

Test developed and characteristics determined by ARUP Laboratories. See Compliance Statement B: aruplab.com/CS