

Client: Example Client ABC123
123 Test Drive
Salt Lake City, UT 84108
UNITED STATES

Physician: Doctor, Example

Patient: Patient, Example

DOB: 12/21/1966
Gender: Female
Patient Identifiers: 01234567890ABCD, 012345
Visit Number (FIN): 01234567890ABCD
Collection Date: 00/00/0000 00:00

MLH1 Promoter Methylation

ARUP test code 3004308

MLH1 Promoter Methylation

Positive *

MLH1 promoter methylation was detected.

This result has been reviewed and approved by [REDACTED]
M.D.

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.

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.

Block ID

S23-5130 A10

H=High, L=Low, *=Abnormal, C=Critical

Mismatch Repair by Immunohistochemistry with Reflex to MLH1 Promoter Methylation

ARUP test code 2005270

Mismatch Repair by IHC Result

Abnormal

Abnormal immunohistochemical staining for mismatch repair proteins correlates well with the presence of microsatellite instability by PCR. The MLH1 Promoter Methylation test (2002499) may be helpful in distinguishing sporadic from Lynch (HNPCC) associated non-colorectal cancers with abnormal MLH1 immunostaining. Controls worked appropriately.

This result has been reviewed and approved by [REDACTED], M.D.

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 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.

Mismatch Repair by IHC with MLH1 **Abnormal**

Mismatch Repair by IHC with MSH2 **Normal**

Mismatch Repair by IHC with MSH6 **Normal**

Mismatch Repair by IHC with PMS2 **Abnormal**

Client Case or Ref # [REDACTED]

H=High, L=Low, *=Abnormal, C=Critical

MSI Tissue Source

Uterus

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
MLH1 Promoter Methylation	23-128-155747	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Block ID	23-128-155747	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Mismatch Repair by IHC Result	23-128-155747	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Mismatch Repair by IHC with MLH1	23-128-155747	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Mismatch Repair by IHC with MSH2	23-128-155747	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Mismatch Repair by IHC with MSH6	23-128-155747	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Mismatch Repair by IHC with PMS2	23-128-155747	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Client Case or Ref #	23-128-155747	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
MSI Tissue Source	23-128-155747	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00

END OF CHART

H=High, L=Low, *=Abnormal, C=Critical

Unless otherwise indicated, testing performed at:

ARUP LABORATORIES | 800-522-2787 | aruplab.com
500 Chipeta Way, Salt Lake City, UT 84108-1221
Jonathan R. Genzen, MD, PhD, Laboratory Director

Patient: Patient, Example
ARUP Accession: 23-128-155747
Patient Identifiers: 01234567890ABCD, 012345
Visit Number (FIN): 01234567890ABCD
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