ARUP LABORATORIES
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Jonathan R. Genzen, MD, PhD, Chief Medical Officer

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

Physician: Doctor, Example

Patient: Patient, Example

DOB	10/1/1936
Gender:	Male
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	00/00/0000 00:00

BRAF Codon 600 Mutation Detection with Reflex to MLH1 Promoter Methylation

ARUP test code 0051750

BRAF codon 600 Mutation Detection	**Positive** *

A mutation in BRAF codon 600 was detected: c.1799T>A, p.V600E

This result has been reviewed and approved by [redacted]

INTERPRETIVE INFORMATION: BRAF codon 600 Mutation Detection with Reflex to MLH1 Promoter Methylation

Presence of a BRAF c.1799T>A, p.Val600Glu (V600E) mutation in a microsatellite unstable colorectal carcinoma indicates that the tumor is probably sporadic and not associated with Lynch syndrome (HNPCC). However, if a BRAF mutation is not detected, the tumor may either be sporadic or Lynch syndrome associated. It should be noted that there have been rare reports of BRAF mutations in Lynch syndrome associated tumors, so the presence of a BRAF mutation does not completely exclude the possibility of Lynch syndrome.

Methodology:
DNA is isolated from microdissected tumor tissue and amplified for exon 15 of the BRAF gene. Mutation status is determined by pyrosequencing.

Limitations: Mutations in other locations within the BRAF gene or in other genes will not be detected.
Limit of detection: 10 percent mutant alleles.

Clinical Disclaimer: 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.

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	SX23-3602 B3

Mismatch Repair by Immunohistochemistry with Reflex to BRAF Codon 600 Mutation and MLH1 Promoter Methylation

ARUP test code 2002327

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

Mismatch Repair by IHC, Result	Abnormal 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 [redacted] M.D. INTERPRETIVE INFORMATION: Mismatch Repair by IHC, Result 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]
MSI Tissue Source	R Colon

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

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
BRAF codon 600 Mutation Detection	23-123-156796	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Block ID	23-123-156796	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Mismatch Repair by IHC, Result	23-123-156796	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Mismatch Repair by IHC with MLH1	23-123-156796	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Mismatch Repair by IHC with MSH2	23-123-156796	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Mismatch Repair by IHC with MSH6	23-123-156796	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Mismatch Repair by IHC with PMS2	23-123-156796	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Client Case or Ref #	23-123-156796	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
MSI Tissue Source	23-123-156796	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