MAYO CLINIC LABORATORIES

Test Definition: BRAFD

BRAF V600E/V600K Somatic Mutation Analysis, Tumor

Overview

Useful For

Therapy selection for patients with cancer (eg, melanomas that may respond to BRAF inhibitors, colon cancers that may not respond to EGFR inhibitors)

Aiding in the diagnosis/prognosis of certain cancers (eg, hairy cell leukemia, papillary thyroid cancers, and association with aggressiveness)

Aiding in determining risk for Lynch syndrome (eg, an adjunct to negative *MLH1* germline testing in cases where colon tumor demonstrates MSI-H and loss of MLH1 protein expression)

This test is **not intended** as a screening test to identify cancer.

Genetics Test Information

This test evaluates tumor DNA for the presence of *BRAF* V600E or V600K mutations in patients with cancer and can be used to determine if these patients are candidates for targeted therapies.

Additional Tests

Test Id	Reporting Name	Available Separately	Always Performed
SLIRV	Slide Review in MG	No, (Bill Only)	Yes

Testing Algorithm

When this test is ordered, slide review will always be performed at an additional charge.

For more information see Lynch Syndrome Testing Algorithm.

Special Instructions

- Lynch Syndrome Testing Algorithm

Method Name

Droplet Digital Polymerase Chain Reaction (ddPCR)

NY State Available

Yes

Specimen

Specimen Type

Varies

Necessary Information

1. A pathology report (final or preliminary) is required and must accompany specimen for testing to be performed.

2. The following information must be included in the report provided.

-Patient name

-Block number-**must be on all blocks, slides and paperwork** (can be handwritten on the paperwork)

-Date of tissue collection

-Source of the tissue

Specimen Required

Preferred: Submit **both** of the following specimens.

Acceptable: Submit **at least** one of the following specimens.

Specimen Type: Tissue block

Collection Instructions: Submit a formalin-fixed, paraffin-embedded tissue block with acceptable amount of tumor tissue.

Specimen Type: Tissue slide

Slides: 1 Hematoxylin and eosin-stained and 5 unstained

Collection Instructions:

Submit the following slides:

1 slide stained with hematoxylin and eosin

AND

5 unstained, nonbaked slides with 5-micron thick sections of the tumor tissue

Note: The total amount of required tumor nuclei can be obtained by scraping up to 5 slides from the same block.

Additional Information:

1. Hematoxylin and eosin-stained and unstained slides will not be returned.

2. Broken or cracked unstained slides will be rejected. Stained slides that were broken and repaired (ie, double mounted) at the client site will not be rejected, as, in most cases, they can still be reviewed under the microscope. However, due to the double mounting, digital scanning cannot be performed.

Forms

If not ordering electronically, complete, print, and send an Oncology Test Request (T729) with the specimen.

Specimen Minimum Volume

See Specimen Required

Reject Due To

Broken or cracked unstained slides	Reject
Broken or	Reject

cracked stained slides that cannot be repaired	

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Ambient (preferred)		
	Refrigerated		

Clinical & Interpretive

Clinical Information
This test assesses for somatic (tumor-specific) *BRAF* V600E and V600K mutation. The *BRAF* gene is a member of the mitogen-activated protein/extracellular signal-regulated (MAP/ERK) kinase pathway, which plays a role in cell proliferation and differentiation. Dysregulation of this pathway is a key factor in tumor progression and *BRAF* mutations occur frequently in many different tumor types. *BRAF* mutation analysis aids in the diagnosis of cancer types including anaplastic and papillary thyroid carcinoma, hairy cell leukemia, and papillary craniopharyngioma.

BRAF V600E and V600K mutations are associated with response or resistance to specific targeted therapies in cancer. Targeted cancer therapies are defined as antibody or small molecule drugs that block the growth and spread of cancer by interfering with specific cell molecules involved in tumor growth and progression. Multiple targeted therapies have been approved by the US Food and Drug Administration for treatment of specific cancers. Molecular genetic profiling is often needed to identify targets amenable to targeted therapies and to minimize treatment costs and therapy-associated risks.

BRAF mutation analysis can provide helpful diagnostic information in the context of evaluation for Lynch syndrome. For more information see Lynch Syndrome Testing Algorithm.

Reference Values
An interpretive report will be provided.

Interpretation
The interpretation of molecular biomarker analysis includes an overview of the results and the associated diagnostic, prognostic, and therapeutic implications.

Cautions
Not all tumors that have *BRAF* mutations respond to *BRAF*-targeted therapies.

Rare genetic alterations (ie, polymorphisms) exist that could lead to false-negative or false-positive results.

This assay was designed to detect *BRAF* c.1799T>A (V600E) and c.1798_1799delGTinsAA (V600K) alterations. The

sensitivity for rarer V600 alterations has not been established.

Test results should be interpreted in context of clinical findings, tumor sampling, and other laboratory data. If results obtained do not match other clinical or laboratory findings, please contact the laboratory for possible interpretation. Misinterpretation of results may occur if the information provided is inaccurate or incomplete.

Reliable results are dependent on adequate specimen collection and processing. This test has been validated on formalin-fixed, paraffin-embedded tissues; other types of fixatives are discouraged. Improper treatment of tissues, such as decalcification, may cause polymerase chain reaction failure.

Colon cancer is relatively common, and it is possible for a sporadic colon cancer to occur in a Lynch syndrome family. Therefore, evaluation of other family members should still be considered in cases with *MLH1* promoter hypermethylation and absence of the *BRAF* V600E mutation if there is high clinical suspicion of Lynch syndrome.

This test is not validated for serial monitoring of patients with cancer.

This test cannot differentiate between somatic and germline alterations. Additional testing may be necessary to clarify the significance of results if there is a potential hereditary risk.

Broken or cracked unstained slides are not compatible with the instrumentation used in our performing laboratories and will be rejected. Additional material may be requested.

Attempts will be made to repair broken or cracked stained slides; however, if they are unable to be repaired (ie, shattered in transit), they will be rejected and discarded due to safety concerns.

Clinical Reference

1. Chapman PB, Hauschild A, Robert C, et al. BRIM-3 Study Group. Improved survival with vemurafenib in melanoma with BRAF V600E mutation. N Engl J Med. 2011;364(26):2507-2516
2. Di Nicolantonio F, Martini M, Molinari F, et al. Wild-type BRAF is required for response to panitumumab or cetuximab in metastatic colorectal cancer. J Clin Oncol. 2008;26(35):5705-5712
3. Hyman DM, Puzanov I, Subbiah V, et al. Vemurafenib in multiple nonmelanoma cancers with BRAF V600 mutations. N Engl J Med. 2015;373(8):726-736
4. Domingo E, Laiho P, Ollikainen M, et al. BRAF screening as a low-cost effective strategy for simplifying HNPCC genetic testing. J Med Genet. 2004;41(9):664-668

Performance

Method Description

Droplet digital polymerase chain reaction-based assay to detect the presence of the *BRAF* V600E and *BRAF* V600K alterations.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed
Varies

Report Available
6 to 12 days

Specimen Retention Time
Tissue blocks: Unused portions of blocks will be returned; Tissue slides: Hematoxylin and eosin-stained and unstained slides will not be returned. Unused slides are stored for at least 5 years.

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Main Campus

Fees & Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification
This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information
81210
88381-Microdissection, manual

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
BRAFD	BRAF V600 Somatic Mutation Analysis, Tumor	97025-1

Result ID	Test Result Name	Result LOINC® Value
608306	Result Summary	50397-9
608307	Result	97025-1
608308	Interpretation	69047-9
608309	Additional Information	48767-8
608310	Specimen	31208-2
608311	Source	31208-2

608312	Released By	18771-6
608235	Method	85069-3
608222	Tissue ID	80398-1
606746	Disclaimer	62364-5