Test Definition: MELP

Melanoma Panel, Tumor

Overview

Useful For

Diagnosis and management of patients with melanoma

Simultaneously interrogating multiple gene targets including *BRAF* (eg, V600E and V600K), *GNAQ*, *GNA11*, *KIT* and *NRAS*

Genetics Test Information

This test uses targeted next-generation sequencing to evaluate for somatic mutations within the *BRAF* (exons 11 and 15), *GNAQ* (exon 5), *GNA11* (exon 5), *KIT* (exon 2, 9, 10, 11, 13, 14, 15, 17, 18), and *NRAS* (exons 2, 3, 4) genes. This includes, but is not limited to, the testing of somatic mutations in *NRAS* codons 12, 13, 61,146; *GNA11* and *GNAQ* codon 209; and *BRAF* codons 594, 596, 600 (e.g. V600E/K). See Targeted Gene Regions Interrogated by Melanoma Panel in Special Instructions for details regarding the targeted gene regions identified by this test.

Additional Tests

Test ID	Reporting Name	Available Separately	Always Performed
SLIRV	Slide Review in MG	No	Yes

Testing Algorithm

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

Special Instructions

- Targeted Gene Regions Interrogated by Melanoma Panel
- Tissue Requirements for Solid Tumor Next-Generation Sequencing

Method Name

Polymerase Chain Reaction (PCR)-Based Next Generation Sequencing

NY State Available

Yes

Specimen

Specimen Type

Varies

Advisory Information

Mutations in genes interrogated by this test can be seen in neoplasms other than melanoma. For *KIT* Asp816Val mutation analysis in mast cell disease, see KITAS / *KIT* Asp816Val Mutation Analysis, Qualitative PCR, Varies.

Necessary Information

Pathology report (final or preliminary) at minimum containing the following information must accompany specimen in order for testing to be performed:

1. Patient name

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

3. Tissue collection date

4. Source of the tissue

Specimen Required

This assay requires at least 20% tumor nuclei.

-Preferred amount of tumor area with sufficient percent tumor nuclei: tissue144 mm(2)

-Minimum amount of tumor area: tissue 36 mm(2).

-These amounts are cumulative over up to 10 unstained slides and must have adequate percent tumor nuclei.

-Tissue fixation: 10% neutral buffered formalin, not decalcified

-For specimen preparation guidance, see Tissue Requirement for Solid Tumor Next-Generation Sequencing in Special Instructions. In this document, the sizes are given as 4mm x 4mm x 10 slides as preferred: approximate/equivalent to 144 mm(2) and the minimum as 3mm x 1mm x 10 slides: approximate/equivalent to 36mm(2).

Preferred:

Specimen Type: Tissue block

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

Acceptable:

Specimen Type: Tissue slide

Slides: 1 stained and 10 unstained

Collection Instructions: Submit 1 slide stained with hematoxylin and eosin and 10 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 10 slides from the same block.

Specimen Type: Cytology slide (direct smears or ThinPrep)

Slides: 1 to 3 slides

Collection Instructions: Submit 1 to 3 slides stained and cover slipped with a preferred total of 5000 nucleated cells or a minimum of at least 3000 nucleated cells.

Note: Glass coverslips are preferred; plastic coverslips are acceptable but will result in longer turnaround times.

Additional Information: Cytology slides will not be returned.

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

Other	Specimens that have been decalcified (all methods) Specimens that have not been formalin-fixed, paraffin-embedded

Specimen Stability Information

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

Clinical and Interpretive

Clinical Information

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 FDA 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.

Next generation sequencing has recently emerged as an accurate, cost-effective method to identify mutations across numerous genes known to be associated with response or resistance to specific targeted therapies. This test is a single assay that uses formalin-fixed paraffin-embedded tissue to assess for common mutations in the following genes known to be associated with melanoma: *BRAF, GNA11, GNAQ, KIT,* and *NRAS*. This includes the common *BRAF* V600E and V600K mutations. The results of this test can be useful for assessing prognosis and guiding treatment of individuals with melanoma.

See Targeted Gene Regions Interrogated by Melanoma Panel in Special Instructions for details regarding the targeted gene regions identified by this test.

Reference Values

An interpretative report will be provided.

Interpretation

An interpretive report will be provided.

Cautions

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. DNA variants of uncertain significance may be

identified.

A negative (wild-type) result does not rule out the presence of a mutation that may be present but below the limits of detection of this assay (approximately 5%-10%). This test does not detect large single or multiexon deletions or duplications or genomic copy number variants.

Rare polymorphisms may be present that could lead to false-negative or false-positive results. Test results should be interpreted in the context of clinical findings, tumor sampling and other laboratory data. If results obtained do not match other clinical or laboratory findings, contact the laboratory for updated 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 PCR failure.

Clinical Reference

1. Carvajal RD, Antonescu CR, Wolchok JD, et al: KIT as a therapeutic target in metastatic melanoma. JAMA 2011;305(22):2327-23342. Postow MA, Carvajal RD: Therapeutic implications of KIT in melanoma. Cancer J 2012;2:137-141

3. Johnson DB, Sosman JA: Update on the targeted therapy of melanoma. Curr Treat Options Oncol 2013;2:280-292

4. Anderson S, Bloom K, Vallera D, et al: Multisite analytic performance studies of a real-time polymerase chain reaction assay for the detection of BRAF V600E mutations in formalin-fixed paraffin-embedded tissue specimens of malignant melanoma. Arch Pathol Lab Med 2012 Nov;136(11):1385-1391

5. Chapman P, 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 Jun 30;364(26):2507-2516

6. Dhomen N, Marais R: BRAF signaling and targeted therapies in melanoma. Hematol Oncol Clin North Am 2009 Jun;23(3):529-545

7. Flaherty K, Puzanov I, Kim K, et al: Inhibition of mutated, activated BRAF in metastatic melanoma. N Engl J Med 2010 Aug 26;363(9):809-819

8. Ascierto P, Schadendorf D, Berking C, et al: MEK162 for patients with advanced melanoma harbouring NRAS or Val600 BRAF mutations: a non-randomised, open-label phase 2 study. Lancet Oncol 2013 Mar;14(3):249-256

9. Jakob J, Bassett R, Ng C, et al: NRAS Mutation status is an independent prognostic factor in metastatic melanoma. Cancer 2012 Aug 15;118(16):4014-4023

10. Van Raamsdonk C, Griewank K, Crosby M, et al: Mutations in GNA11 in uveal melanoma. N Engl J Med 2010 Dec 2;363(23):2191-2199

11. Kusters-Vandevelde H, Klaasen A, Kusters B, et al: Activating mutations of the GNAQ gene: a frequent event in primary melanocytic neoplasms of the central nervous system. Acta Neuropathol 2010 Mar;119(3):317-323

12. Griewank K, van de Nes J, Schilling B, et al: Genetic and clinico-pathologic analysis of metastatic uveal melanoma. Mod Pathol 2014 Feb;27(2):175-183

Performance

Method Description

Next generation sequencing is performed to test for the presence of a mutation in targeted regions of the *BRAF, GNA11, GNAQ, KIT,* and *NRAS* genes. See Targeted Gene Regions Interrogated by Melanoma Panel in Special Instructions for details regarding the targeted gene regions identified by this test.(Unpublished Mayo method)

PDF Report

No

Day(s) and Time(s) Test Performed

Monday through Friday; Varies

Analytic Time

12 days

Maximum Laboratory Time

20 days

Specimen Retention Time

Unused portions of blocks will be returned. Unused slides are stored indefinitely.

Performing Laboratory Location

Rochester

Fees and 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 Regional Manager. 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. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information

81445

88381-Microdissection, manual

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
MELP	Melanoma Panel, Tumor	In Process

Result ID	Test Result Name	Result LOINC Value
54879	Result Summary	50397-9
54880	Result	82939-0

Test Definition: MELP

Melanoma Panel, Tumor

Result ID	Test Result Name	Result LOINC Value
54881	Interpretation	69047-9
54882	Additional Information	48767-8
54884	Specimen	31208-2
54885	Source	31208-2
54886	Tissue ID	80398-1
54887	Released By	18771-6