MAYO CLINIC LABORATORIES

Test Definition: KRASP

KRAS Somatic Mutation Analysis, Tumor

Overview

Useful For

Detecting molecular markers associated with response or resistance to specific cancer 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.

Special Instructions

- Molecular Genetics: Inherited Cancer Syndromes Patient Information

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 3, if available, or 2 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 10 unstained
Collection Instructions:
Submit the followings slides:
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.
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.

Specimen Type: Cytology slide (direct smears or ThinPrep)
Slides: 1 to 3 Slides
Collection Instructions: Submit 1 to 3 slides stained and coverslipped with a total of 5000 nucleated cells (preferred), or at least 3000 nucleated cells (minimum).
Note: Glass coverslips are preferred; plastic coverslips are acceptable but will result in longer turnaround times.
Additional Information:
1. Cytology slides will not be returned.
2. 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

1. Molecular Genetics: Inherited Cancer Syndromes Patient Information (T519).
2. If not ordering electronically, complete, print, and send a Oncology Test Request (T729) with the specimen.

Specimen Minimum Volume

See Specimen Required

Reject Due To

Broken or cracked unstained slides	Reject
Broken or cracked stained slides that cannot be repaired	Reject

Specimen Stability Information

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

Clinical & Interpretive

Clinical Information

Strategies that focus on early detection and prevention effectively decrease the risk of mortality associated with cancer. In addition, an increase in survival rate for individuals with advanced stage disease has been observed as a result of advancements in standard chemotherapeutic agents and the development of specialized targeted therapies. Monoclonal antibodies against epidermal growth factor receptor (EGFR), such as cetuximab and panitumumab, represent an area of targeted therapy for patients with colorectal and non-small cell lung cancer (NSCLC). However, studies have shown that not all individuals with colorectal cancer or NSCLC respond to EGFR targeted molecules. Because the combination of targeted therapy and standard chemotherapy leads to an increase in toxicity and cost, strategies that help to identify the individuals most likely to benefit from such targeted therapies are desirable.

Epidermal growth factor receptor is a growth factor receptor that is activated by the binding of specific ligands (epiregulin and amphiregulin), resulting in activation of the RAS/MAPK pathway. Activation of this pathway induces a signaling cascade ultimately regulating a number of cellular processes including cell proliferation. Dysregulation of the RAS/MAPK pathway is a key factor in tumor progression. Targeted therapies directed to EGFR, which inhibit activation of the RAS/MAPK pathway, have demonstrated some success (increased progression-free and overall survival) in patients with cancer, in particular, colorectal cancer and NSCLC.

One of the most common somatic mutations in colon cancer and NSCLC is the presence of activating mutations in the protooncogene *KRAS*. *KRAS* is recruited by ligand-bound (active) EGFR to initiate the signaling cascade induced by the RAS/MAPK pathway. Because altered *KRAS* constitutively activates the RAS/MAPK pathway downstream of EGFR, agents such as cetuximab and panitumumab, which prevent ligand-binding to EGFR, do not appear to have any meaningful inhibitor activity on cell proliferation in the presence of altered *KRAS*. Current data suggest that the efficacy of EGFR-targeted therapies in colon cancer and NSCLC is confined to patients with tumors lacking *KRAS* mutations. An exception is the *KRAS* G12C variant, which is targetable with variant-specific inhibitors.

This test uses DNA extracted from tumor tissue to evaluate for the presence of *KRAS* (G12A, G12C, G12D, G12R, G12S, G12V, G13D, Q61K, Q61L, Q61R, Q61H, and A146T) mutations. A positive result indicates the presence of an activating *KRAS* mutation and can be a useful marker by which patients are selected for EGFR-targeted therapy.

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 patients whose tumors have wildtype *KRAS* respond to epidermal growth factor receptor (EGFR)-targeted therapies.

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

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.

This assay was designed to detect variants in *KRAS* codons 12, 13, 61, and 146 (G12A, G12C, G12D, G12R, G12S, G12V, G13D, Q61K, Q61L, Q61R, Q61H, and A146T).

This test has not been clinically validated for use as a tool to monitor response to therapy or for early detection of tumors.

This test cannot differentiate between somatic and germline alterations.

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.Allegra CJ, Rumble BR, Hamilton SR, et al. Extended RAS gene mutation testing in metastatic colorectal carcinoma to predict response to anti-epidermal growth factor receptor monoclonal antibody therapy: ASCO Provisional Clinical Opinion update 2015. J Clin Oncol. 2016;34(2):179-185
2.Spano JP, Milano G, Vignot S, Khayat D. Potential predictive markers of response to EGFR-targeted therapies in colorectal cancer. Crit Rev Oncol Hematol. 2008;66(1)21-30
3.Lam DC: Clinical testing for molecular targets for personalized treatment in lung cancer. Respirology. 2013;18(2):233-237
4.Hong DS, Fakih MG, Strickler JH, et al. KRAS G12C inhibition with sotorasib in advanced solid tumors. N Engl J Med. 2020;383(13):1207-1217

Performance

Method Description

A pathology review and macrodissection to enrich for tumor cells is performed prior to DNA extraction.

Droplet digital polymerase chain reaction is used to test for the presence of *KRAS* codon 12, 13, 61, and 146 variants.(Unpublished Mayo method).

PDF Report

No

Day(s) Performed
Monday through Friday

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; Extracted DNA: 3 months

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
81275-KRAS (v-Ki-ras2 Kirsten rat sarcoma viral oncogene) (eg, carcinoma) gene analysis, variants in codons 12 and 13
81276-KRAS additional variant(s)
88381-Microdissection, manual

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
KRASP	KRAS Somatic Mutation Analysis	103955-1

Result ID	Test Result Name	Result LOINC® Value
610680	Result Summary	50397-9
610681	Result	82939-0
610682	Interpretation	69047-9
610683	Specimen	31208-2
610684	Source	31208-2
610685	Tissue ID	80398-1
610686	Released By	18771-6
610687	Method	85069-3

610688	Disclaimer	62364-5
614165	Additional Information	48767-8