MAYO CLINIC LABORATORIES

Test Definition: KRASD

Cell-Free DNA KRAS 12, 13, 61,146, Blood

Overview

Useful For

An alternative to invasive tissue biopsies for the determination of *KRAS* 12, 13, 61,146 (G12A, G12C, G12D, G12R, G12S, G12V, G13D, Q61K, Q61L, Q61R, Q61H, and A146T) mutation status

Detecting molecular markers associated with response or resistance to specific therapy

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

Genetics Test Information

This test evaluates cell-free DNA (cfDNA) in the peripheral blood for the presence of *KRAS* mutations at codons 12, 13, 61, and 146 (G12A, G12C, G12D, G12R, G12S, G12V, G13D, Q61K, Q61L, Q61R, Q61H, and A146T) in patients with cancer and can be used to assess eligibility for targeted therapies.

Highlights

This test provides rapid detection of *KRAS* mutations in colorectal cancer patients as an alternative for KRAS analysis of tissue.

Current data suggests that the efficacy of epidermal growth factor receptor (EGFR)-targeted therapy in colorectal cancer patients is limited to patients whose tumors do not harbor mutations in the *KRAS* gene.

Method Name

Digital Droplet Polymerase Chain Reaction (PCR)

NY State Available

Yes

Specimen

Specimen Type

Whole blood

Ordering Guidance

This test is **not** a prenatal screening test

Shipping Instructions

1. Samples should be transported at ambient temperature or refrigerated (4 degrees C).
2. Samples are viable for 7 days in the Streck Black/Tan Top Tube Kit (T715).

Specimen Required

Supplies: Streck Black/Tan Top Tube Kit (T715)

Container/Tube: Streck Cell-Free DNA blood collection kit
Specimen Volume: Two 10-mL Streck Cell-Free DNA blood collection tubes
Additional Information: Only blood collected in Streck Cell-Free DNA BCT tubes will be accepted for analysis. Whole blood will be processed to produce platelet-poor plasma before cfDNA isolation.

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

Specimen Minimum Volume
One 10 mL Streck tube

Reject Due To

Specimen collected in tube other than Streck Cell-Free DNA collection tube	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole blood	Ambient (preferred)	7 days	Streck Black/Tan top
	Refrigerated	7 days	Streck Black/Tan top

Clinical & 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 US Food and Drug Administration for treatment of solid tumor malignancies. Molecular genetic profiling is often needed to identify targets amenable to targeted therapies and to minimize treatment costs and therapy-associated risks.

One of the most common somatic alterations in colorectal cancer (CRC) and non-small cell lung cancer (NSCLC) is the presence of activating variants in the protooncogene *KRAS*. *KRAS* is recruited by ligand-bound (active) epidermal growth factor receptor (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 CRC and NSCLC is confined to patients with tumors lacking KRAS mutations. An exception is the *KRAS* G12C variant that 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) variants. A positive result indicates the presence of an activating KRAS mutation and can be useful for guiding the treatment of patients with CRC and NSCLC.

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

Patients with a negative test result may still harbor a KRAS mutation. Mutation testing of a tissue specimen for KRAS mutations should be considered for patients with who have a negative result with this test.

The limit of detection of this assay for the detection of KRAS mutations is influenced by the amount of cell-free DNA (cfDNA) in the blood. This is a biological variable that cannot be controlled.

This assay was designed to detect mutations 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. Additional testing may be necessary to clarify the significance of results if there is a potential hereditary risk.

Supportive Data

This test has been evaluated by our laboratory as an alternative to assessing paraffin-embedded tumor specimens for *KRAS* mutations in patients with colorectal cancer.

Clinical Reference

1. Schwarzenbach H, Hoon DS, Pantel K. Cell-free nucleic acids as biomarkers in cancer patients. Nat Rev Cancer. 2011;11(6):426-437
2. 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: American Society of Clinical Oncology Provisional Clinical Opinion Update 2015. J Clin Oncol. 2016;34(2):179-185. doi:10.1200/JCO.2015.63.967
3. Olmedillas Lopez S, Garcia-Olmo DC, Garcia-Arranz M, et al. KRAS G12V mutation detection by droplet digital PCR in circulating cell-free DNA of colorectal cancer patients. Int J Mol Sci. 2016;17(4):484
4.Lam DC. Clinical testing for molecular targets for personalized treatment in lung cancer. Respirology. 2013 Feb;18(2):233-237
5.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
Blood samples are collected in Streck Cell-Free DNA BCT tubes. Cell-free DNA (cfDNA) is isolated from double-spun plasma and assessed for the presence of *KRAS* codon 12, 13, 61, and 146 mutations using droplet digital polymerase chain reaction.(Unpublished Mayo method)

PDF Report
No

Day(s) Performed
Varies

Report Available
5 to 10 days

Specimen Retention Time
Whole Blood: 2 weeks (if available); 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
81276

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
KRASD	cfDNA KRAS 12, 13, 61, 146 Blood	In Process

Result ID	Test Result Name	Result LOINC® Value
113123	Result Summary	50397-9
113125	Interpretation	69047-9
113126	Additional Information	48767-8

113127	Specimen	31208-2
113128	Source	31208-2
113129	Released By	18771-6
113508	Result	75974-6