Test Definition: KRASC

KRAS Mutation Analysis, Colorectal

Overview

Useful For

Prognostic markers for cancer patients treated with epidermal growth factor receptor-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.

Special Instructions

- Molecular Genetics: Inherited Cancer Syndromes Patient Information
- Informed Consent for Genetic Testing

Method Name

Polymerase Chain Reaction (PCR) Analysis

NY State Available

Yes

Specimen

Specimen Type

Varies

Specimen Required

Pathology report**must** accompany specimen in order for testing to be performed.

Preferred:

Specimen Type: Tissue

Container/Tube: Tissue block

Collection Instructions: Submit a formalin-fixed, paraffin-embedded tissue block.

Acceptable:

Specimen Type: Tissue

Container/Tube: Slides

Specimen Volume: 1 stained and 5 unstained

Collection Instructions: Submit 1 slide stained with hematoxylin and eosin and 5 unstained, nonbaked slides with 5 micron-thick sections of the tumor tissue.

Forms

1. Molecular Genetics: Inherited Cancer Syndromes Patient Information (T519) in Special Instructions.

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

Specimen Minimum Volume

Formalin-fixed, paraffin-embedded (FFPE) tissue block (preferred) or 1 slide stained with hematoxylin-and-eosin and 5 unstained, nonbaked slides (5-microns thick sections) of the tumor tissue.

Reject Due To

Hemolysis	NA
Lipemia	NA
Icterus	NA
Other	Specimens that have been decalcified (all methods); specimens that have not been formalin-fixed, paraffin-embedded; bone marrow in EDTA

Specimen Stability Information

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

Clinical and Interpretive

Clinical Information

Colorectal cancer is currently among the most common malignancies diagnosed each year. Strategies that focus on early detection and prevention effectively decrease the risk of mortality associated with the disease. In addition, an increase in survival rate for individuals with advanced stage colorectal cancer 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 a new area of targeted therapy for such patients. However, studies have shown that not all individuals with colorectal cancer 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.

EGFR 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 colorectal cancer.

One of the most common somatic alterations in colon cancer is the presence of activating mutations in the proto-oncogene *KRAS*. *KRAS* is recruited by ligand-bound (active) EGFR to initiate the signaling cascade induced by the RAS/MAPK pathway. Because mutant *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 mutant *KRAS*. Current data suggest that the efficacy of EGFR-targeted therapies in colon cancer is confined to patients with tumors lacking *KRAS* mutations. As a result, the mutation status of *KRAS* can be a useful marker by which patients are selected for EGFR-targeted therapy.

At this time, this test is approved specifically for colorectal tumors and metastatic lesions from a colorectal primary. Refer to KRASO / *KRAS* Mutation Analysis, 7 Mutation Panel, Other (Non-Colorectal) for *KRAS* testing in noncolorectal tumors.

Reference Values

An interpretative report will be provided.

Interpretation

An interpretative report will be provided.

Cautions

Not all patients who have wild-type *KRAS* respond to epidermal growth factor receptor (EGFR)-targeted therapies.

Clinical Reference

1. Khambata-Ford S, Garrett CR, Meropol NJ, et al: Expression of Epiregulin and Amphiregulin and K-ras mutation status predict disease control in metastatic colorectal cancer patients treated with Cetuximab. J Clin Oncol 2007;25:3230-3237

2. Lievre A, Bachet JB, Le Corre D, et al: KRAS mutation status is predictive of response to Cetuximab therapy in colorectal cancer. Cancer Res 2006;66(8):3992-3995

3. 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;66:21-30

Performance

Method Description

A PCR-based assay employing Scorpions real-time PCR and allele-specific PCR technologies is used to test for 7 mutations within codons 12 and 13 of the *KRAS* gene (G12D, G12A, G12V, G12S, G12R, G12C, and G13D).(Package insert: therascreen KRAS RGQ PCR Kit. Qiagen, Manchester, UK; July 2012)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

5 to 7 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 has been cleared, approved or is exempt by the U.S. Food and Drug Administration and is used per manufacturer's instructions. Performance characteristics were verified by Mayo Clinic in a manner consistent with CLIA requirements.

CPT Code Information

81275-KRAS (v-Ki-ras2 Kirsten rat sarcoma viral oncogene) (eg, carcinoma) gene analysis, variants in codons 12 and 13

Additional Test

88381-Microdissection, manual

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
KRASC	KRAS Mutation Analysis, Colorectal	85509-8

Result ID	Test Result Name	Result LOINC Value
53273	Result Summary	50397-9
53274	Result	82939-0
53275	Interpretation	69047-9
53276	Specimen	31208-2
53277	Source	31208-2
54445	Tissue ID	80398-1
53278	Released By	18771-6