KRAS

Mutation Analysis Result Report

PATIENT/ID		SPECIMEN		PHYSICIAN	
Patient:	Jane Doe	Requisition:	DP 90022403	Ordering Physician:	James Edney, MD
DOB:	31-Oct-1963	Collection Date:	25-Mar-2012	Ordering Facility:	Univ. of Nebraska Med. Ctr
Patient #:	024836267	Date Received:	25-Mar-2012	Address:	42nd and Emile
Gender:	Female	Report Date:	29-Mar-2012	City, St., Zip:	Omaha, NE 68198
Customer Ref.:		Tumor Origin:	Colon	Country:	

KRAS Mutation Analysis Result:

MUTATION DETECTED

A point mutation affecting codon 12 of the *KRAS* gene was detected (p.Gly12Asp, c.35G>A).

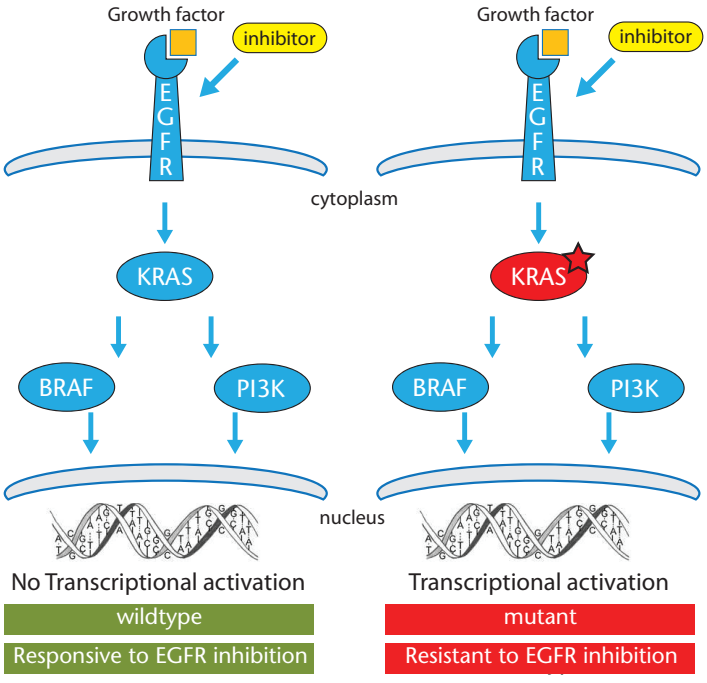
Clinical Relevance/Comments:

KRAS is associated with the downstream signaling pathway of EGFR and is mutated in 35-45% of colorectal cancer (CRC), 10-30% of non-small cell lung cancer (NSCLC) and frequently in other cancers[1,8].

Targeted EGFR therapies include monoclonal antibodies (e.g., cetuximab, panitumumab) that can prevent ligand binding and EGFR activation, or tyrosine kinase inhibitors (TKI, e.g. erlotinib) that prevent activation of the signaling pathways. KRAS mutations can interfere with this mode of action.

The presence of a KRAS mutation predicts that the patient is unlikely to benefit from targeted EGFR therapy in colon cancer[2-7], head-and neck cancer[10] and in lung cancer [7-9]. Targeted EGFR therapy can be considered in patients with a wild-type KRAS gene. MEK inhibitors are emerging as an important drug class to consider for KRAS mutant patients[13].

The results of this test are to be interpreted in the context of other clinical findings in patient care management.



National Comprehensive Cancer Network (NCCN) guidelines for colon cancer recommend, with a category 2A, the testing of all metastatic disease for the presence of mutations in KRAS[11-12]. An American Society of Clinical Oncology (ASCO) provisional clinical opinion also recommended that patients with metastatic colorectal cancer who are candidates for anti-EGFR targeted therapy should be tested for KRAS mutational status at codons 12 and 13[3].

NCCN guidelines for NSCLC recommends KRAS mutation testing category 2B. NCCN further recommends alternative therapies be considered for patients with KRAS mutations[9,12].

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decoding cancer

KRAS

Mutation Analysis Result Report

PATIENT/ID **Patient:** Jane Doe | **DOB:** 31-Oct-1963 | **Patient #:** 024836267 | **Report Date:** 25-Mar-2012

Methodology:

This assay qualitatively detects mutations in DNA of the *KRAS* gene using mutation specific primers in combination with real time PCR. Tumor areas were identified, and when necessary selectively macrodissected. This highly sensitive PCR assay is capable of reproducibly detecting mutations in samples with as little as 1 to 5% mutated DNA. The assay is validated on DNA isolated from FFPE tissue. Primers were designed so that known variants do not interfere with mutation detection; however, the presence of previously unknown variants might interfere with assay performance on rare occasions.

Assay Description:

This test detects nucleotide variants affecting codons 12 and 13 of the *KRAS* gene:

- p.Gly12Ala, c.35G>C;
- p.Gly12Asp, c.35G>A;
- p.Gly12Arg, c.34G>C;
- p.Gly12Cys, c.34G>T;
- p.Gly12Ser, c.34G>A;
- p.Gly12Val, c.35G>T;
- p.Gly13Asp, c.38G>A;

Intended Use:

The therascreen KRAS RGQ PCR Kit (Qiagen) is intended to aid in the identification of colorectal cancer patients suited for treatment with Erbitux® (cetuximab) based on a KRAS wildtype test result.

References:

1. Tan C, et al. KRAS mutation testing in metastatic colorectal cancer. World J Gastroenterol. 2012 Oct 7; 18(37):5171-80.
2. Amado RG et al. Wildtype KRAS is required for panitumumab efficacy in patients with metastatic colorectal cancer. J Clin Oncol. 2008; 26:1626-1634.
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7. Linardou H, et al. Assessment of somatic k-ras mutations as a mechanism associated with resistance to EGFR-targeted agents: a systematic review and meta-analysis of studies in advanced non-small-cell lung cancer and metastatic colorectal cancer. Lancet Oncol. 2008;9:962-972.
8. Eberhard DA, et al. Mutations in the epidermal growth factor receptor and in KRAS are predictive and prognostic indicators in patients with non-small-cell lung cancer treated with chemotherapy alone and in combination with erlotinib. J Clin Oncol. 2005;25:5900-5909.
9. NCCN Clinical Practice Guidelines in Oncology™. Non-small-cell lung cancer. v1.2013. http://www.nccn.org/professionals/physician_gls/PDF/nscl.pdf. Last accessed December 11, 2012.
10. Smilek P, et al. Epidermal growth factor receptor (EGFR) expression and mutations in the EGFR signaling pathway in correlation with anti-EGFR therapy in head and neck squamous cell carcinomas. Neoplasma. 2012;59(5):508-15.
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13. http://www.asco.org/ASCOv2/Meetings/Abstracts?&vmview=abst_detail_view&confID=114&abstractID=98430.

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Sign Off
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Pathologist

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