KRAS/BRAF Mutation Analysis

ONCOLOGY

KRAS/BRAF Mutations and Cancer

The *KRAS* gene encodes a small GTPase that plays a key role in transducing signals from the epidermal growth factor receptor (EGFR) to downstream effectors. *KRAS* mutations have been commonly found in several types of human malignancies, such as metastatic colorectal cancer (mCRC), lung adenocarcinoma and thyroid cancer. Activating mutations are commonly found in exon 2 (codon 12/13), exon 3 (codon 61), and exon 4 (codon 117/146).

Several studies have demonstrated that tumors carrying any of these mutant forms of the KRAS gene are less likely to respond to anti-EGFR antibody therapy. The American Society of Clinical Oncology (ASCO) recently released its first Provisional Clinical Opinion (PCO) suggesting that all patients to be administered anti-EGFR monoclonal antibody and tyrosine kinase inhibitor therapies (e.g. cetuximab, panitumumab, gefitinib and erlotinib) should be screened for *KRAS* mutations.

Recent studies have also shown that not all mCRC patients with wild-type *KRAS* tumors respond to anti-EGFR therapy. This suggests that additional genes and/or pathways may be involved in the mechanism of resistance to these drugs. Mutations in exon 4 of KRAS, as well as exon 15 of BRAF, another downstream effector of the EGF-activated pathway, have been identified in up to 15% of mCRC tumors. Patients with these activating mutations have decreased progression-free (PFS) and overall (OS) survival when treated with EGFR antagonists.

These findings strongly suggest that screening for both KRAS and BRAF mutations is necessary to more accurately identify patients who will not respond to anti-EGFR therapy.

Testing Procedure and Analysis

EntroGen's *KRAS/BRAF* mutation panel is a polymerase chain reaction (PCR)-based assay and uses allele-specific primers to identify the presence of mutations in *KRAS* codons 12, 13, 61, 117 and 146 as well as *BRAF* V600E (also available separately). The testing procedure involves three (3) simple steps:

- Isolation of DNA from tumor biopsies, paraffin-embedded sections (FFPE), or fresh frozen tumors
- Amplification of regions of the *KRAS* and *BRAF* genes using allele-specific primers
- Detection of amplification product on a Real-Time PCR instrument.

This test can be completed in approximately 2 hours from isolation of DNA to test result.

Equipment and Materials

EntroGen's *KRAS/BRAF* mutation panel requires a real-time PCR instrument capable of detecting FAM and VIC fluorescent probes.

This test includes reagents required for the PCR amplification/detection, as well as validated reaction controls. Columns and reagents for DNA isolation are not included.

Intended Use

EntroGen's *KRAS/BRAF* mutation analysis kits are available for Research Use Only (RUO) in the United States and for In Vitro Diagnostic use (CE-IVD) in Europe.

Ordering Information

Product Name	Cat. No.
K-Ras Mutation Analysis Kit for Real-Time PCR (exons 2, 3 & 4)	KRAS-RT50
B-Raf Mutation Analysis Kit for Real-Time PCR (exon 15)	BRAF-RT50
K-Ras/B-Raf Mutation Analysis Kit for Real-Time PCR (exons 2, 3 & 4 of KRAS and exon 15 of BRAF)	KRBR-RT50

20950 Warner Center Ln Ste B • Woodland Hills, CA 91367 • (818) 716-1070 • www.entrogen.com