# KRAS Mutation Detection

**Clinical Significance**:

Multiple studies have now shown that patients with tumors harboring mutations in KRAS or NRAS exons 2, 3, or 4 predict lack of response to anti-EGFR antibody therapy given in combination with chemotherapy (Ciardiello et al. 2014; Douillard et al. 2013; Karthaus et al. 2013; Peeters et al. 2014; Stintzing et al. 2014; Tejpar et al. 2014).
Approximately 36–40% of patients with colorectal cancer have tumor-associated KRAS mutations (Amado et al. 2008; COSMIC; Faulkner et al. 2010; Neumann et al. 2009). The concordance between primary tumor and metastases is high (Cejas et al. 2009; Mariani et al. 2010; Santini et al. 2008), with only 3–7% of the tumors discordant. The majority of the mutations occur at codons 12, 13, and 61 of the KRAS gene. The result of these mutations is constitutive activation of KRAS signaling pathways. Multiple studies have now shown that patients with tumors harboring mutations in KRAS are unlikely to benefit from anti-EGFR antibody therapy, either as monotherapy (Amado et al. 2008) or in combination with chemotherapy (Bokemeyer et al. 2009; Bokemeyer et al. 2011; Douillard et al. 2010; Lievre et al. 2006; Peeters et al. 2010). Further, in trials of oxaliplatin based chemotherapy, the patients with KRAS mutated tumors appeared to do worse when treated with EGFR antibody therapy combined with an oxaliplatin based chemotherapy compared to the patients treated with an oxaliplatin based treatment alone.

**Testing Method:** The activating (hot spot) mutations in KRAS codons 12,13, 61 and 146 are detected by DNA based next generation sequencing.**Test Parameters:** The limit of detection of this assay has been determined to be approximately 5% of mutant allele(s) in the background of wild type allele.

**Turnaround Time:** 5-7 business days

**Sample Requirements**: The presence of adequate tumor in the material submitted for analysis should be confirmed by a surgical pathologist. A section from archival paraffin material or frozen surgical biopsies should be confirmed to contain > 50% tumor by a surgical pathologist. If the submitted material for analysis contains < 50% of tumor, areas of predominant tumor will be macrodissected using a scalpel to enrich neoplastic cells.

- Formalin-fixed, paraffin-embedded tissue
- 5-6 tissue sections (please include H&E slide and a copy of pathology report)
- Cytology samples
- Fresh frozen tissue

**CPT Codes:** 81276, 88381 may apply

Ship Specimens to:

Henry Ford Center for Precision Diagnostics
Henry Ford Hospital
Clinic Building, K6, Core Lab E-655
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