

KRAS Mutation Detection in Colorectal Carcinoma

Overview

August, 2009

PathGroup Labs is pleased to announce the immediate availability of the *KRAS* Mutation Detection Assay for Colorectal Carcinoma. This assay detects all possible mutations in codons 12 and 13 of the *KRAS* gene in colorectal carcinoma specimens.

The protein encoded by the *KRAS* gene functions in the signal transduction pathway downstream of the Epidermal Growth Factor Receptor (EGFR). Current anti-EGFR therapies, such as cetuximab and panitumumab, block activation of EGFR. Tumors that have somatic mutations that activate the *KRAS* protein have been hypothesized to be refractory to anti-EGFR therapy, since the activated *KRAS* protein provides a pro-growth and pro-survival signal downstream of the EGFR therapy target. Recent randomized control trials as well as retrospective studies have confirmed that this is the case.

The American Society for Clinical Oncology (ASCO) has recently released a Provisional

Clinical Opinion (PCO) regarding *KRAS* mutation testing in colorectal carcinoma. This PCO states that patients that are candidates for anti-EGFR therapy should have *KRAS* mutational analysis performed, and if the tumor is *KRAS* mutant, anti-EGFR therapy is contraindicated.

The PathGroup *KRAS* Mutation Detection Assay is performed on formalin-fixed paraffin embedded tissue specimens. Tumor tissue of interest is marked by a pathologist and micro-dissected from surrounding normal tissue. Genomic DNA is isolated from the selected tumor tissue and analyzed by PCR and Pyrosequencing. Pyrosequencing is a state of the art technology that provides gold standard sequence data with an analytic sensitivity of 5-10%. This assay will detect all possible mutations in codons 12 and 13 of the *KRAS* gene, which represents greater than 98% of known activating *KRAS* mutations.

Clinical Utility

- Determination of appropriateness of anti-EGFR therapy in patients with colorectal carcinoma.

Methodology: Genomic DNA is isolated from micro-dissected tumor tissue. The *KRAS* gene is PCR amplified and analyzed using Pyrosequencing specific for codons 12 and 13.

Test Codes: KRAS

CPT Codes: 88381, 83891, 83907, 83898, 83896, 83904, 83912

Specimen Collection: One H&E stained slide with the tumor area of interest circled, and the corresponding paraffin-embedded tissue block for this slide. Approximately 50 mm² of tumor area (at 5 micron thickness) is required for analysis.

Shipping and Handling: Handle unstained slides with care (especially on uncharged slides) to keep tissue from being disturbed. Ship all slides to histology (for deparaffinization and rehydration) at room temperature.

Reference Ranges: Mutation Not Detected

Turnaround Time: 5-7 days. (Assay is performed on Thursdays)

References

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