TriCores' molecular diagnostic laboratory offers an efficient and cost-effective targeted sequencing panel for mutations in key genes (*KRAS*, *NRAS*, *BRAF*, *PIK3CA*) relating to prognosis and therapy response in colorectal carcinoma.

The anti-epidermal growth factor receptor (EGFR) antibodies cetuximab and panitumumab are currently approved for treatment of metastatic colorectal cancer in patients without *KRAS* mutations. Although the vast majority of *RAS* mutations, rendering resistance to EGFR-targeted agents, occur in *KRAS* exon 2 (codons 12 and 13), recent studies revealed that approximately 20% of *KRAS* exon 2 wild type tumors harbored a mutation in *KRAS* or *NRAS* exons 3 or 4. Recent data suggest that these mutations can also be associated with resistance to anti-EGFR antibodies and hence support expanded *RAS* mutation analysis. Currently the definition of expanded *RAS* includes *KRAS* and *NRAS* codons 12 and 13 (exon 2), 59 and 61 (exon 3), and 117 and 146 (exon 4),[1] as specified by draft guidelines of the joint ASCO/ASCP/CAP/AMP panel on molecular markers in colorectal carcinoma. Furthermore, the recently updated National Comprehensive Cancer Network (NCCN) guidelines clearly state that "all patients with metastatic colorectal cancer should have tumor tissue genotyped for *RAS* mutations (*KRAS* and *NRAS*). Patients with any *KRAS* mutation (exon 2 or non-exon2) or *NRAS* mutation should not be treated with either cetuximab or panitumumab."[2]

In order to efficiently analyze the indicated exons, TriCore uses the Ion Torrent next generation sequencing platform from Life Technologies. The sequencing power available using this technology also allows for easy and cost-effective examination of two additional genes relevant to colorectal cancer treatment. The *BRAF* V600E mutation is a strong prognostic marker, and *BRAF* analysis is recommended in certain patients by NCCN guidelines and by the joint ASCO/ASCP/CAP/AMP draft guidelines. Somatic mutations in *PIK3CA* have been found in 10-30% of colorectal cancers. Some studies, but not others, have suggested that *PIK3CA* mutations are prognostic and predictive in this setting.[3, 4]

For additional information, please contact TriCore's molecular diagnostics laboratory at 505-938-8684.

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REFERENCES

[1] Atreya CE, Corcoran RB, Kopetz S: J Clin Oncol 2015; 33: 682-5.

[2] National Comprehensive Cancer Network Guidelines Version 3.2015 Colon Cancer

[3] Liao X, Morikawa T, Lochhead P, et al. Clin Cancer Res 2012; 18: 2257–68.

[4] Karapetis CS et al. Clin Cancer Res 2014; 20: 744-53.

TriCore
REFERENCE LABORATORIES

COLORECTAL CANCER MUTATION PANEL (*KRAS, NRAS, BRAF, PIK3CA*)

Test Code.........................MDCOL
CPT Code.........................81275, 81404x2, 81210, G0452-26
Methodology....................Next Generation Sequencing
Test Includes.....................*KRAS, NRAS, BRAF, PIK3CA*

Related Documents.........................Solid Tumor Requisition
Testing Performed...........................Friday
Reported...Reported in 7 days

COLLECTION

Collection Instructions	Test is ordered by the molecular diagnostic laboratory and resulted in PowerPath. Include surgical pathology report. Send requisition with specimen to molecular diagnostics laboratory.
Specimen	Preferred: Tissue (formalin-fixed, paraffin-embedded block) Acceptable: Tissue (paraffin-embedded section)
Rejection Criteria	Tissue specimens with no tumor, frozen specimens and specimens fixed/processed in alternative fixatives (alcohol Prefer®) or fixatives containing heavy metals are unacceptable.

PROCESSING

Specimen Processing Instructions	Paraffin-embedded, formalin-fixed tissue block or unstained 5µm slides, preferably 6 slides. If the specimen to be tested is a needle biopsy or contains less than 50% tumor, send 10 unstained 5µm slides.

SHIPPING/TRANSPORT AND STORAGE

Stabilities/Storage: (*Collection to initiation of testing*)	**Temperature** Ambient Refrigerated Frozen	**Stability** Indefinite Indefinite Unacceptable
Shipping Instructions	Ship ambient. Protect paraffin block from excessive heat. Ship in cooled container during the summer months.	