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.

For consultation, please contact:
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Dr. David Czuchlewski  505-938-8467  dczuchlewski@salud.unm.edu

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

<table>
<thead>
<tr>
<th>Test Code</th>
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<tr>
<td>CPT Code</td>
<td>81275, 81404x2, 81210, G0452-26</td>
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<tr>
<td>Methodology</td>
<td>Next Generation Sequencing</td>
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<tr>
<td>Test Includes</td>
<td>KRAS, NRAS, BRAF, PIK3CA</td>
</tr>
</tbody>
</table>

**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:**
- **Temperature:** Ambient, Refrigerated
- **Stability:** Indefinite, Indefinite

**Shipping Instructions**
Ship ambient. Protect paraffin block from excessive heat. Ship in cooled container during the summer months.