

The UT Genetics Center laboratories are directed by experienced medical professionals who are board certified by the American Board of Medical Genetics in the specialties of clinical cytogenetics, clinical molecular genetics and clinical biochemical genetics. Genetic counseling/consultation is provided by board certified or board eligible physicians and counselors.

The UT Genetics Center accepts all private and commercial insurance plans, Medicare, and TennCare insurance. Payment in cash or by credit card is also accepted. The Genetics Center participates in the Knoxville Academy of Medicine sponsored program for uninsured patients, and recognizes eligibility evaluations of area hospitals and clinics for sliding scale payments.

Contact the UT Genetics Center Laboratories at 865-305-9449 for information on specific test offerings, specimen requirements, and pick up/delivery

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KRAS Gene Mutation Analysis

Will your patient's colorectal tumor be resistant to EGFR-based chemotherapy?



University of Tennessee
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Laboratories

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Why are KRAS mutations significant for patient oncology management?

In November of 2008, the NCCN recommended that the KRAS gene status of colorectal tumors be assessed prior to the initiation of monoclonal antibody based epidermal growth factor receptor (EGFR) targeted treatments.

KRAS (k-Ras kinase) is a component of the EGFR pathway and recent studies have shown that colorectal tumors with KRAS mutations are *resistant* to monoclonal antibody EGFR targeted chemotherapy agents. **Therefore, patients whose tumors are positive for KRAS mutations have a poor prognosis in relation to monoclonal antibody EGFR-based therapies.** KRAS mutation analysis offers refinement to the treatment decision-making process by separating patients according to the likely response to these agents.

The high cost of monoclonal antibody EGFR-based therapies in addition to the time lost due to the use of a potentially inefficient treatment in cases with KRAS mutations indicate that this knowledge has significant clinical utility.

The UT Genetics Center Laboratories currently offers KRAS mutation analysis for colorectal tumor types only. However, studies are emerging that KRAS mutation status may also be relevant for additional tissue types including non-small cell lung and pancreatic tumors. Therefore, additional tumor types may be added to the acceptable tissue samples list in the future.

Specimen Submission Requirements

Option 1—Colorectal Tumors: Unstained Slides:*

- Slides cut within 5-7 days are preferred; older slides may be used but may not provide as successful an analysis.
- Minimum of 3 slides from a slide sequence that has been confirmed by a pathologist to contain significant numbers of tumor cells**
- Pre-cut slides from paraffin block in 7 micron sections.
- Air dry. Do not oven dry.
- Store specimen at room temperature (20-23.5°C).
- Turn around time: 5-7 days.

Option 2—Colorectal Tumors: Formalin-fixed, Paraffin-embedded Block*

- Tissues should be well-fixed in formalin. If an alternative fixative is used, it should be noted on the requisition.
- Pathologist must have determined that the block contains significant numbers of tumor cells.**
- Store specimen at room temperature (20-23.5°C).
- Use cold pack for extended transport. Be sure cold pack is not in direct contact with specimen during transport.
- Turn around time: 5-7 days.

*Specimens must be accompanied by test requisition, copies of insurance documentation and a signed ABN form when appropriate. Analysis cannot be performed unless all required information is provided.

**Sensitivity of the assays is *critically linked* to the enrichment of tumor cells in the provided specimen.

Possible Test Results

- **Positive:** KRAS gene mutations at codons 12/13 or codon 61 of exon I are present; which suggests that this patient is unlikely to respond favorably to treatment with monoclonal antibody EGFR-based therapies.
- **Negative/Not Detected:** KRAS gene mutations in codons 12/13 or 61 of exon I not detected.
 - Negative results may occur if insufficient tumor cells are present in the tumor specimen.
 - Negative test results do not guarantee that the tumor will be sensitive to antibody based treatments as other factors may also be involved in regulation of this sensitivity.
 - Additional mutations are known to be present in a small percentage of tumors. Development of analysis for these mutations is in process

Sensitivity of the assays is *critically linked* to the enrichment of tumor cells in the provided specimen.

