

NRAS Mutation Detection in Melanoma and Colorectal Cancer

FOR HELPING PREDICT PATIENT RESPONSE TO EGFR INHIBITORS FOR COLORECTAL CANCER AND TO DRUGS TARGETED AT GENES DOWNSTREAM OF NRAS IN THE MITOGEN ACTIVATION PROTEIN KINASE (MAPK) SIGNALING CASCADE FOR MALIGNANT MELANOMA

Test Highlights

- NRAS mutational status may indicate a tumor that will respond to drugs targeted at genes downstream of NRAS in the mitogen activating protein kinase (MAPK) signaling cascade for malignant melanoma.
- Mutations in this gene can also inhibit therapeutic response to EGFR-targeted therapies in patients with metastatic colorectal cancer.

Disease Overview

- Melanoma is a cancer that arises from melanocytes, specialized pigmented cells that are found predominantly in the skin. The incidence of melanoma is rising steadily in Western populations; the number of cases worldwide has doubled in the past 20 years.
- In the United States, colorectal cancer is the third most common form of cancer; individuals have a 6 percent lifetime risk of developing this disease.
- Most colorectal cancer is caused by somatic mutations and is not hereditary.
- Mutations in the oncogene NRAS are present in about 15 percent of human tumors.

Indications for Ordering

- NRAS mutations may indicate a tumor that will not respond to anti-EGFR therapies (as in colon cancer).
- NRAS mutations may indicate a tumor that will respond to drugs targeted at genes downstream of NRAS in the MAPK signaling cascade (as in melanoma).

Interpretation

- The presence of an oncogenic mutation in codons 12, 13, or 61 of NRAS is indicative of a tumor that may respond to drugs targeted at genes downstream of NRAS in the mitogen activating protein kinase (MAPK) signaling cascade.
- Mutations in this gene may also indicate tumors (e.g., metastatic colorectal cancer) that will not respond to EGFR-targeted therapies.

Methodology

- Tumor tissue is microdissected and DNA extracted from five micron sections of formalin-fixed, paraffin-embedded tissue blocks.
- Regions covering codons 12, 13, and 61 of the NRAS gene are amplified using polymerase chain reaction (PCR), followed by pyrosequencing.

- All potentially oncogenic mutations in codons 12,13, and 61 are detected.
- Limit of detection for this assay is 10 percent mutant alleles.

Limitations

- Mutations in other locations within the NRAS gene or in any other gene will not be detected.
- Absence of NRAS mutations does not guarantee a positive response to anti-EGFR therapies in metastatic colorectal cancer.
- The presence of mutations in codons 12, 13, or 61 does not guarantee a positive response to therapies in melanoma.

References

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Test Information

2003123 *NRAS* Mutation Detection, Pyrosequencing

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For information on test selection, ordering, and interpretation, refer to ARUP Consult® at www.arupconsult.com.