NRAS Mutation Analysis

CERNER ORDERABLE
Using IU Health Pathology requisition; Order through CoPath please call 317.491.6417

CPT CODE
81311

CLINICAL UTILITY
The Neuroblastoma RAS (NRAS) gene is in the RAS family of oncogenes, which also includes two other genes: HRAS and KRAS. It is located at chromosome 1p13.2 and encodes for a 21 kDa protein with GTPase activity. GTPase plays an important role in cell division, cell differentiation, and the self-destruction of cells (apoptosis). The proteins functions as mediators of cellular growth signals generated by upstream receptor tyrosine kinases and transduced to the nucleus through the MAPK pathway2. Oncogenic mutations of RAS family members are one of the most common genetic lesions in cancer. These mutations interfere with the ability of NRAS to hydrolyze GTP to GDP forcing NRAS to remain constitutively active. Oncogenic mutations in NRAS are observed in multiple types of carcinomas including melanoma, leukemia's, thyroid carcinomas, lung cancers and colon cancers. Mutations of NRAS are found in approximately 20% of melanomas, 12% of acute myeloid leukemias, 8% of thyroid carcinomas, and 2-3% of colon cancers5.The majority of NRAS mutations are observed in melanoma, thyroid and colorectal cancers occur at codon 61, while the NRAS mutations in hematopoietic malignancies are consistently distributed between multiple codons. Mutations in the NRAS gene are associated with resistance to anti-epidermal growth factor receptor (EGFR) therapies in colorectal cancers withour KRAS mutations. In melanoma, NRAS mutations predict a positive response to MEK-targeted agents, such as trametinib and selumetinib.

METHODOLOGY
NRAS mutation analysis using the Qiagen NRAS Pyro® kits on the Q24 Pyrosequencer allows for quantitative measurement of NRAS mutations that mainly exist in exons 2, 3 and 4. Mutations in codons 12/13, 59, 61, 117, and 146 are detected by PCR amplification followed by pyrosequencing through defined regions in the forward direction10. Extracted DNA specimens are amplified in a PCR step, immobilized using Streptavidin Sepahrose beads, prepared as single-stranded DNA and annealed to specific sequencing primer, and then analyzed on the PyroMark Q24 in order to determine the presence/absence of specific NRAS mutations.

SPECIMENS
Preferable primary tumor.

- FFPE tissue (Formalin fixative only), cell block FNAs
  For tissue resection: 1 H&E and 8 unstained slides
  For a biopsy: 1 section on 1 slide for H&E plus 6 unstained slides with 3 sections/ slide

SPECIMEN STABILITY and SHIPPING

- Transport/Storage of slides at room temperature.

CAUSES FOR REJECTION
Excess necrosis for slides. Inadequate percentage tumor; poor DNA quality.

ASSAY RANGE

- NRAS mutation not detected.
- NRAS mutation detected.

TURNAROUND TIME 7-10 Working days

1. Reference information can be found in the Indiana University Health Molecular Assay Procedures.