NRAS Mutation Detection, Pyrosequencing

Metastatic melanoma is associated with a poor prognosis and poor response to traditional chemotherapy or radiation therapy, as is metastatic CRC. Targeted therapy may play a role in treatment of disseminated disease. Genetic variants guide utilization of targeted therapy for melanoma (BRAF, NRAS, KIT) and CRC (BRAF, KRAS, NRAS). NRAS mutation detection screens for individuals with melanoma who may respond to therapy targeted at downstream genes in the MAPK signaling pathway and screens for individuals with CRC who may show relative resistance to anti-EGFR therapies. (For more information, see the Colorectal Cancer - Predictive Testing for Anti-EGFR Therapy Test Fact Sheet).

Genetics

Gene

NRAS

Structure/Function

GTPase-encoding gene in the RAS/RAF/MAPK pathway

Mutations

- Majority of activating mutations are in exon 2 (codons 12 and 13) and exon 3 (codon 61).
- NRAS, KRAS, and BRAF mutations are mutually exclusive in individuals with CRC.
- NRAS mutations rarely overlap with BRAF and KIT mutations in melanoma.
- Guidelines suggest extended RAS testing in CRC, which includes codons 12, 13, 59, 61, 117, and 146.

Test Interpretation

Sensitivity/Specificity

Clinical Sensitivity

Activating NRAS mutations are found in 20% of metastatic melanomas and ~3% of CRCs.

Analytical Sensitivity/Specificity

100%

Results

<table>
<thead>
<tr>
<th>Result</th>
<th>Variant(s) Detected</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>Oncogenic NRAS mutation detected</td>
<td>Predictive of relative resistance to anti-EGFR therapy in CRC. Possibly predictive of response to therapy targeted at downstream genes in the MAPK signaling pathway in melanoma.</td>
</tr>
<tr>
<td>Negative</td>
<td>No oncogenic NRAS mutation detected</td>
<td>n/a</td>
</tr>
</tbody>
</table>

Limitations

- Limit of detection: 10% mutant alleles
- Does not cover extended RAS; oncogenic mutations outside of codons 12, 13, and 61 will not be detected.
Presence or absence of mutations does not guarantee a response or lack of response to anti-EGFR therapies or therapies targeted at downstream genes in the MAPK signaling pathway.

References


Related Information

Melanoma
Colorectal (Colon) Cancer
Colorectal Cancer - Predictive Testing for Anti-EGFR Therapy

Related Tests

BRAF Codon 600 Mutation Detection by Pyrosequencing 2002498
Method: Polymerase Chain Reaction/Pyrosequencing

BRAF V600E Mutation Detection in Circulating Cell-Free DNA by Digital Droplet PCR 2013921
Method: Polymerase Chain Reaction

KIT Mutations Melanoma 3004283
Method: Massively Parallel Sequencing

KRAS Mutation Detection 0040248
Method: Polymerase Chain Reaction/Pyrosequencing

Solid Tumor Mutation Panel, Sequencing 3004294
Method: Massively Parallel Sequencing