

NRAS Mutation Detection, Pyrosequencing

Metastatic melanoma is associated with a poor prognosis and poor response to traditional chemotherapy or radiation therapy,¹ as is metastatic CRC.² Targeted therapy may play a role in treatment of disseminated disease. Genetic variants guide utilization of targeted therapy for melanoma (*BRAF*, *NRAS*, *KIT*)³ 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 pathway³ and screens for individuals with CRC who may show relative resistance to anti-EGFR therapies.² (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).⁴
- *NRAS*, *KRAS*, and *BRAF* mutations are mutually exclusive in individuals with CRC.⁵
- *NRAS* mutations rarely overlap with *BRAF* and *KIT* mutations in melanoma.³
- Guidelines suggest extended *RAS* testing in CRC, which includes codons 12, 13, 59, 61, 117, and 146.²

Test Interpretation

Sensitivity/Specificity

Clinical Sensitivity

Activating *NRAS* mutations are found in 20% of metastatic melanomas⁶ and ~3% of CRCs.

Analytical Sensitivity/Specificity

100%

Results

Result	Variant(s) Detected	Interpretation
Positive	Oncogenic <i>NRAS</i> mutation detected	Predictive of relative resistance to anti-EGFR therapy in CRC ² Possibly predictive of response to therapy targeted at downstream genes in the MAPK signaling pathway in melanoma ³
Negative	No oncogenic <i>NRAS</i> mutation detected	n/a

Tests to Consider

[NRAS Mutation Detection by Pyrosequencing 2003123](#)

Method: Polymerase Chain Reaction/Pyrosequencing

- Use to detect activating *NRAS* mutations (codons 12, 13, 61) associated with relative resistance to anti-EGFR therapy in colorectal cancer (CRC).
- Use to predict response to anti-EGFR and MAPK pathway therapies in a variety of malignancies (eg, melanoma and CRC).

See [Related Tests](#)

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

1. Domingues B, Lopes JM, Soares P, et al. [Melanoma treatment in review](#). *Immunotargets Ther*. 2018;7:35-49.
2. National Comprehensive Cancer Network. [NCCN Clinical Practice Guidelines in Oncology: Colon cancer](#). Version 2.2021. [Updated: Jan 2021; Accessed: Feb 2021]
3. National Comprehensive Cancer Network. [NCCN Clinical Practice Guidelines in Oncology: Melanoma—cutaneous](#). Version 1.2020. [Last update: Jan 2021; Accessed: Feb 2021]
4. Heppt MV, Siepmann T, Engel J, et al. [Prognostic significance of BRAF and NRAS mutations in melanoma: a German study from routine care](#). *BMC Cancer*. 2017;17(1):536.
5. Nagakubo Y, Hirotsu Y, Amemiya K, et al. [Accurate detection of KRAS, NRAS and BRAF mutations in metastatic colorectal cancers by bridged nucleic acid-clamp real-time PCR](#). *BMC Med Genomics*. 2019;12(1):162.
6. Dummer R, Schadendorf D, Ascierto PA, et al. [Binimetinib versus dacarbazine in patients with advanced NRAS-mutant melanoma \(NEMO\): a multicentre, open-label, randomised, phase 3 trial](#). *Lancet Oncol*. 2017;18(4):435-445.

Related Information

[Melanoma](#)
[Colorectal 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

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