Colorectal Cancer Mutation Panel

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BRAF testing and extended *RAS* gene testing (*KRAS* and *NRAS*) are recommended in all patients with colorectal cancer who have been diagnosed with metastatic disease because *BRAF*, *KRAS*, and *NRAS* variants are associated with resistance to anti-epidermal growth factor receptor (anti-EGFR) therapy.[1] This test uses targeted massively parallel sequencing (MPS; also known as next generation sequencing [NGS]) to identify hotspot variants in *BRAF*, *KRAS*, and *NRAS* and can help guide decision-making for targeted therapy.

Featured ARUP Testing

Colorectal Cancer Mutation Panel
3017209

Method: Massively Parallel Sequencing

Recommended test to detect mutations in *BRAF*, *KRAS*, and *NRAS* genes in colorectal cancer (CRC) to determine patient eligibility for targeted therapy.

Disease Overview

Colorectal cancer (CRC), also referred to as colon cancer, is a leading cause of cancer death. CRC screening strategies rely on colonoscopy findings, laboratory test results, or a combination of the two. Laboratory testing may also be used to determine whether certain treatments are likely to be effective.[1] For more information about the recommended testing strategy for CRC, refer to the ARUP Consult Colorectal (Colon) Cancer topic.

Test Interpretation

Genes Tested

Clinically significant single nucleotide variants (SNVs), multiple nucleotide variants (MNVs), and small insertions and deletions (1-25 base pairs [bp]) and variants of uncertain significance within the preferred transcripts of the genes below are reported.

Gene	Transcript (NM)	Covered Exon(s)[a]	Covered Regions
BRAF	NM_004333.4	15[a]	chr7:140453100-140453172
KRAS	NM_004985.4	2[a], 3[a], 4[a]	chr12:25398230-25398318, chr12:25380261-25380349, chr12:25378541-25378683
NRAS[b]	NM_002524.4	2[a], 3[a], 4[a]	chr1:115258706-115258781, chr1:115256488-115256578, chr1:115252188-115252330

[a]Indicated exons are partially covered for hotspots only and not reported in full.

[b]Only SNVs are reported for the indicated gene.

Limitations

- This test does not detect variants in areas outside of the targeted genomic regions or below the limit of detection. Additional evaluation should be considered for complete genetic analysis, including detection of variants outside of the hotspot regions covered by this test, translocations, or gene rearrangements, if clinically indicated.

- Copy number alterations (losses or amplifications), translocations, microsatellite instability, tumor mutational burden, deep intronic variants, insertions/deletions larger than 25bp, and RNA variants are not detected.
- This test evaluates for variants in tumor tissue only and cannot distinguish between somatic and germline variants. If a hereditary/familial cancer is of clinical concern, additional clinical evaluation and genetic counseling should be considered before additional testing.
- In some cases, variants may not be identified due to technical limitations related to the presence of known pseudogenes, GC-rich regions, repetitive or homologous regions, low mappability regions, and/or variants located in regions overlapping amplicon primers.
- Tissue samples yielding between 1ng and 5ng total DNA input may yield suboptimal results and will be accepted for testing with a client-approved disclaimer.
- Benign or likely benign variants in the preferred transcript are not reported.
- Variant allele frequency (VAF) is not reported.
- Results of this test must always be interpreted within the context of clinical findings and other relevant data and should not be used alone for a diagnosis of malignancy, determination of prognosis, or recommendation of therapy.
- This test is not intended to detect minimal residual disease (MRD).

Limit of Detection (LOD)

10% VAF for all variant classes detected by the assay. For variants near the assay LOD, positive percent agreement (PPA) was found to be greater than 90% for all variant classes.

Analytic Accuracy/Sensitivity (PPA)

The PPA estimates for the respective variant classes (with 95 percent credibility region) are listed below.

Variant Class	Analytic Sensitivity (PPA)[a] Estimate (%)	Analytic Sensitivity (PPA)[a] 95% Credibility Region (%)
SNVs	98.4	95.1-99.7
Deletions (1-25bp)	96.8	90.2-99.3
Insertions/duplications (1-25bp)	96.8	90.2-99.3
MNVs	98.2	91.8-99.8

[a]Genes included on this test are a subset of a larger methods-based validation from which the PPA values are derived.

References

1. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology: colon cancer. Version 1.2022. Updated Feb 2022; accessed Oct 2022.

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