BRAF Mutation Detection

Last Literature Review: May 2024 Last Update: May 2024

Testing for *BRAF* mutation status may be useful in certain solid tumors. This test assesses for *BRAF* mutations only; if a more comprehensive evaluation is desired, consider ordering a cancer-specific panel.

Disease Overview

BRAF mutations may be present in different types of solid tumors, such as colorectal cancer, lung cancer, and melanoma. The presence of specific *BRAF* variants may have diagnostic, prognostic, and therapeutic significance in these conditions. *BRAF* testing is indicated in screening for Lynch syndrome and is recommended in all patients with colorectal cancer who have been diagnosed with metastatic disease.[1] For more information about the use of *BRAF* testing in these cancers, refer to the ARUP Consult Colorectal (Colon) Cancer, Melanoma, and Non-Small Cell Lung Cancer topics.

Featured ARUP Testing

BRAF Mutation Detection 3017203

Method: Massively Parallel Sequencing

Use to detect *BRAF* mutations in exon 15, including at codon 600.

BRAF Mutation Detection with Reflex to MLH1 Promoter Methylation 3017204

Method: Massively Parallel Sequencing

Recommended reflex test to differentiate between Lynch syndrome-associated and sporadic colorectal cancer in tumors showing loss of *MLH1*. This test assesses for the *BRAF* V600E variant; if the variant is not present, this test reflexes to *MLH1* promoter methylation testing.

Test Interpretation

Gene Tested

- *BRAF* (NM_004333.4) exon 15 (chr7:140453100-140453172) is evaluated to detect hotspot single nucleotide variants (SNVs), multiple nucleotide variants (MNVs), and small insertions and deletions (1-25 base pairs [bp]). Clinically significant variants and variants of uncertain significance are reported. This exon is partially covered for hotspots only and not reported in full.
- For the reflex test, if the *BRAF* V600E variant is not present, this test reflexes to *MLH1* promoter methylation testing.

Limitations

- This test does not detect variants in areas outside 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 region of *BRAF*, variants within other genes, 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 prior to 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.

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% credibility region) are listed below.

Variant Class	Analytic Sensitivity (PPA)[a] Estimate (%)	Analytic Sensitivity (PPA)[a] 95% Credibility Region (%)
Single nucleotide variants (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
Multiple nucleotide variants (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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