IDH1-IDH2 Mutation Detection

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IDH1 and *IDH2* mutation status may be useful for diagnosis, prognosis, and determination of eligibility for targeted therapy in certain solid tumors. This test uses targeted massively parallel sequencing (MPS; also known as next generation sequencing [NGS]) to identify hotspot variants in *IDH1* and *IDH2* associated with central nervous system tumors and cholangiocarcinoma.

Featured ARUP Testing

IDH1 and IDH2 Mutation Detection 3017222

Method: Massively Parallel Sequencing

Use to detect *IDH1* and *IDH2* mutations.

Disease Overview

IDH1 and *IDH2* mutations may be present in solid tumors including central nervous system tumors such as oligodendrogliomas,[1] cholangiocarcinoma, and other cancers. *IDH* testing is recommended in all gliomas and may be required for appropriate classification.[1] For more specific information about the application of *IDH1* and *IDH2* mutation status testing, refer to ARUP Consult's Primary Brain Tumors – Brain Tumor Molecular Markers topic.

Test Interpretation

Genes Tested

Clinically significant single nucleotide variants (SNVs) and variants of uncertain significance within the preferred transcripts of the genes below are reported. Other types of variants may be reported with a disclaimer, if detected.

Gene	Transcript (NM)	Covered Exon(s)[a]	Covered Regions
IDH1[b]	NM_005896.3	4[a]	chr2:209113083-209113124
IDH2[b]	NM_002168.3	4[a]	chr15:90631809-90631869, chr15:90631901-90631989

[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 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 of *IDH1* or *IDH2*, variants within other genes, gene methylation, translocations, or gene rearrangements, if clinically indicated.
- Copy number alterations (losses or amplifications), translocations, microsatellite instability, tumor mutational burden, deep intronic variants, insertions/deletions, 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 1 ng and 5 ng 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 variants near the assay LOD, positive percent agreement (PPA) was found to be greater than 90%.

Analytic Accuracy/Sensitivity (PPA)

The PPA estimate for the relevant variant class (with 95% credibility region) is listed below. Genes included on this test are a subset of a larger methods-based validation from which the PPA values are derived.

- SNVs: 98.4% (95.1-99.7%)

References

1. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Central nervous system cancers. Version 4.2020. Updated Mar 2021; accessed Mar 2021.