Acute Myeloid Leukemia Mutation Panel by Next Generation Sequencing

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Acute myeloid leukemia (AML) is a myeloid malignancy (ie, a clonal disorder of hematopoietic stem and progenitor cells). Recent studies have identified recurrently mutated genes with diagnostic and/or prognostic significance in AML. The presence of certain variants may inform clinical management.

This multigene panel by massively parallel sequencing (MPS; also referred to as next generation sequencing [NGS]) detects molecular changes including single nucleotide variants (SNVs), small insertions and deletions (indels) relevant to AML. This test is more cost effective than the use of multiple single gene tests and can be used to complement the morphologic and cytogenetic workup of AML.

Featured ARUP Testing

Acute Myeloid Leukemia Mutation Panel by Next Generation Sequencing 3002714

Method: Massively Parallel Sequencing

For more information on ARUP's myeloid malignancies panel, which test the genes in this panel and additional genes relevant to other myeloid malignancies, refer to the Myeloid Malignancies Mutation and Copy Number Variation Panel by Next Generation Sequencing Test Fact Sheet.

For more information on ARUP's targeted rapid turnaround AML panel, which includes some of the genes on this panel, refer to the Rapid Acute Myeloid Leukemia Targeted Therapy Mutation Panel Test Fact Sheet.

For information on other ARUP tests relevant to AML, including information on single-gene tests, refer to the Acute Myeloid Leukemia Molecular Genetic Testing Test Fact Sheet.

For more information on ARUP's genomic microarray testing in oncology, refer to the Cytogenomic Microarray - Oncology Test Fact Sheet.

Disease Overview

Diagnostic, Prognostic, and Treatment Issues

Identification of one or more clonal genetic abnormalities, variants, or patterns of variants in patients with AML may:

- Aid in establishing the diagnosis and subclassification
- Aid in determination of prognosis
- Inform clinical management

For more information about the recommended testing strategy for AML, refer to the ARUP Consult Acute Myeloid Leukemia – AML topic.

Genetics

Genes Tested

ANKRD26, *ASXL1*, *CEBPA*, *DDX41*, *DNMT3A*, *ETV6*, *FLT3*, *GATA2*, *IDH1*, *IDH2*, *KIT*, *KRAS*, *NPM1*, *NRAS*, *RUNX1*, *TP53*, *WT1*

For some genes, one or more exons of the preferred transcript are not covered by sequencing for the indicated gene. Refer to the Genes Tested table below for full list of targeted regions and exclusions.

Test Interpretation

Results

Reported variants are classified into two categories:

- Tier 1: Mutations with known clinical significance in hematologic malignancies
- Tier 2: Variants of unknown clinical significance in hematologic malignancies

Limitations

Limit of Detection

- SNVs and small variants <24 base pair (bp): 5% variant allele fraction (VAF)
- Variants >24 bp: may be detected at limit of detection (LOD), but analytic sensitivity may be reduced

Variants That Will Not Be Detected

- Variants in regions that are not included in the preferred transcript for the targeted genes
  - Refer to the Genes Tested table below for full list of targeted regions and exclusions.
- Copy number variants (losses or gains)
- Loss of heterozygosity
- RNA variants
- Gene fusions, balanced translocations, and other structural variants
- Some variants may not be identified due to technical limitations in the presence of pseudogenes or in repetitive or homologous regions.

Variants That Will Not Be Reported

Benign or likely benign variants in the preferred transcript

Additional Limitations

- This test is not intended to detect minimal residual disease (MRD).
- Interpretation of this test result may be impacted if this patient has had an undisclosed allogeneic bone marrow transplant or stem cell transplant.
- This test does not distinguish between somatic and germline variants.

Analytic Sensitivity

Variant Class	Analytic Sensitivity (PPA)[a] Estimate (%)	Analytic Sensitivity (PPA) 95% Credibility Region[a] (%)
SNVs	96.9	95.1-98.1
Insertions/duplications (1-24 bp)	98.1	95.5-99.3
Insertions/duplications (>24 bp)	>99	92.9-100.0
Deletions (1-24 bp)	96.7	92.8-98.7
Deletions (>24 bp)	90	79.5-96.1
MNVs	97	93.0-99.0
FLT3 ITDs	>99	97.1-100.0

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

bp, base pairs; ITDs, internal tandem duplications; MNVs, multinucleotide variants; PPA, positive percent agreement

Genes Tested

Genes Tested by Acute Myeloid Leukemia Mutation Panel by Next Generation Sequencing	
Gene	Preferred Transcript[a,b]
ANKRD26	NM_014915
ASXL1	NM_015338

Gene	Preferred Transcript[a,b]
CEBPA	NM_004364
DDX41	NM_016222
DNMT3A	NM_175629
ETV6	NM_001987
FLT3	NM_004119
GATA2	NM_032638
IDH1	NM_005896
IDH2	NM_002168
KIT	NM_000222
KRAS	NM_004985
NPM1[c]	NM_002520
NRAS	NM_002524
RUNX1	NM_001754
TP53	NM_000546
WT1	NM_024426

[a]This is the transcript number used for analyzing and reporting variants. The transcript version number may change periodically and thus is not listed here. The transcript with version number will be included on the patient's report if a variant is detected in the gene.

[b]Noncoding exons are not analyzed, except for regions containing known clinically relevant variants in the *ANKRD26* 5′UTR.

[c]Exon 1 is excluded due to technical limitations of the assay.

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