

Chronic Lymphocytic Leukemia Mutation Panel by Next Generation Sequencing

Chronic lymphocytic leukemia (CLL) is a hematopoietic disorder characterized by chronic monoclonal B-cell proliferation. Recent studies have identified recurrently mutated genes with diagnostic and/or prognostic impact in CLL and other lymphoid malignancies. The presence of certain mutations may inform clinical management. This multigene panel by massively parallel sequencing (next generation sequencing) is a more cost-effective approach when compared to the cost of multiple single gene tests. This test can be used to complement the morphologic and cytogenetic workup of CLL and other lymphoid malignancies.

Featured ARUP Testing

[Chronic Lymphocytic Leukemia Mutation Panel by Next Generation Sequencing 3001858](#)

Method: Massively Parallel Sequencing

For more information on the testing strategy for CLL, refer to ARUP Consult's [Chronic Lymphocytic Leukemia](#) topic.

Disease Overview

Diagnostic Issues

- Genetic targets contained in the panel are relevant in CLL and other lymphoid malignancies
- Identification of one or more clonal genetic abnormalities may aid in establishing the diagnosis of a neoplasm, but results must be interpreted within the context of other clinical and hematologic findings
- Identification of certain variants or patterns of variants may aid in prognostication of patients with CLL

Prognostic and Treatment Issues

- Certain variants or patterns of variants may have prognostic significance
- Certain variants may be sensitive to or provide resistance to targeted therapies

Genetics

Genes Tested

ATM, BCL2, BIRC3, BRAF, BTG1, BTK, CARD11, CD79B, CXCR4, DDX3X, FBXW7, IKZF3, KRAS, MAP2K1, MED12, MGA, MYD88, NOTCH1, NRAS, PLCG2, POT1, RNASEH2A, RNASEH2B, RPS15, SAMHD1, SF3B1, TP53, XPO1, ZMYM3

For some genes, one or more exons of the preferred transcript are not covered by sequencing for the indicated gene. See the [Genes Tested](#) table below for full list of targeted regions and exclusions.

Test Interpretation

Results

- Positive: a somatic variant in one of the tested genes was detected
 - Clinical relevance will be described, if known
- Negative: no variants were detected in the sequenced genes

Limitations

- A negative result does not exclude a diagnosis of CLL
- Not intended to detect minimal residual disease (MRD)
- This test does not determine *IGHV* mutation status
- Variants may be present below the limit of detection (LOD) of 5% allele frequency
- Variants greater than 24 base pairs may be detected at LOD, but the analytical sensitivity may be reduced
- Variants may not be identified due to technical limitations in the presence of pseudogenes or in repetitive or homologous regions
- Variants in regions that are not included in the preferred transcript for the targeted genes will not be detected; see [Genes Tested](#) table below for full list of targeted regions and exclusions
- Interpretation of this test result may be impacted if this patient has had an undisclosed allogenic bone marrow transplant or stem cell transplant
- Does not detect translocations, gene rearrangements, copy number alterations, or microsatellite instability
- 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 (1-24bp)	98.1	95.5-99.3
Insertions/duplications (>24bp)	>99	92.9-100.0
Deletions (1-24bp)	96.7	92.8-98.7
Deletions (>24bp)	90	79.5-96.1
MNVs	97	93.0-99.0

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

bp, base pairs; MNVs, multinucleotide variants; PPA, positive percent agreement; SNVs, single nucleotide variants

Genes Tested

Gene	Preferred Transcript ^{a, b}
<i>ATM</i>	NM_000051
<i>BCL2</i>	NM_000633
<i>BIRC3</i>	NM_001165 (exon 5 excluded)
<i>BRAF</i>	NM_004333
<i>BTG1</i>	NM_001731
<i>BTK</i>	NM_000061
<i>CARD11</i>	NM_032415
<i>CD79B</i>	NM_000626
<i>CXCR4</i>	NM_003467
<i>DDX3X</i>	NM_001193416
<i>FBXW7</i>	NM_033632
<i>IKZF3</i>	NM_012481
<i>KRAS</i>	NM_004985
<i>MAP2K1</i>	NM_002755
<i>MED12</i>	NM_005120
<i>MGA</i>	NM_001164273
<i>MYD88</i>	NM_002468
<i>NOTCH1</i>	NM_017617

^aThis 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.

^bNoncoding exons are not analyzed, except for regions containing known clinically relevant variants in the NOTCH1 3'UTR. In addition, coding exons noted here as excluded are not sequenced due to technical limitations of the assay.

Gene	Preferred Transcript ^{a, b}
<i>NRAS</i>	NM_002524
<i>PLCG2</i>	NM_002661
<i>POT1</i>	NM_015450
<i>RNASEH2A</i>	NM_006397
<i>RNASEH2B</i>	NM_024570
<i>RPS15</i>	NM_001018 (exon 3 excluded)
<i>SAMHD1</i>	NM_015474
<i>SF3B1</i>	NM_012433
<i>TP53</i>	NM_000546
<i>XPO1</i>	NM_003400
<i>ZMYM3</i>	NM_201599

^aThis 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.

^bNoncoding exons are not analyzed, except for regions containing known clinically relevant variants in the NOTCH1 3'UTR. In addition, coding exons noted here as excluded are not sequenced due to technical limitations of the assay.

Related Information

Chronic Lymphocytic Leukemia - CLL

ARUP Laboratories is a nonprofit enterprise of the University of Utah and its Department of Pathology. 500 Chipeta Way, Salt Lake City, UT 84108
 (800) 522-2787 | (801) 583-2787 | aruplab.com | arupconsult.com
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