Client: ARUP Example Report Only
500 Chipeta Way
Salt Lake City, UT 84108
UNITED STATES

Physician: EXAMPLE, PHYSICIAN

Patient: MYE CNV, neg example

DOB	
Sex:	Unknown
Patient Identifiers:	54050
Visit Number (FIN):	54438
Collection Date:	10/26/2023 12:22

Myeloid Malignancies Mutation and Copy Number Variation Panel by Next Generation Sequencing

ARUP test code 3016621

MYE CNV Proposed Diagnosis	AML unspec
MYE CNV Specimen	Whole Blood
MYE CNV Interp	See Note

Myeloid Mutation Panel by NGS, DelDup

Submitted diagnosis or diagnosis under consideration for variant interpretation: Acute myeloid leukemia, unspecified (AML, unspec)

Section 1: Molecular Variants

TIER 1: Variants of Known Clinical Significance in Hematologic Malignancies

None found

TIER 2: Variants of Unknown Clinical Significance in Hematologic Malignancies

None found

Section 2: Copy Number Variants and CN-LOH

TIER 1: Variants of Known Clinical Significance in Hematologic Malignancies

None found

TIER 2: Variants of Unknown Clinical Significance in Hematologic Malignancies

None found

This result has been reviewed and approved by [redacted]

Low coverage regions:
Listed below are regions where the average sequencing depth (number of times a particular nucleotide is sequenced) in at least 20% of the region-of-interest is less than our stringent cutoff of 300. Sensitivity for detection of low allelic frequency variants may be reduced in areas with reduced depth of coverage.
None

H=High, L=Low, *=Abnormal, C=Critical

BACKGROUND INFORMATION: Myeloid Malignancies Mutation and Copy Number Variation Panel by Next Generation Sequencing

'CHARACTERISTICS: Myeloid malignancies are clonal disorders of hematopoietic stem and progenitor cells that include myelodysplastic syndromes (MDSs), myeloproliferative neoplasms (MPNs), myelodysplastic/myeloproliferative neoplasms (MDS/MPNs), acute myeloid leukemia (AML), and others. Recent studies have identified recurrently mutated genes with diagnostic and/or prognostic impact in myeloid malignancies. The presence of certain mutations may inform clinical management. This multigene panel by massively parallel sequencing (next generation sequencing) detects molecular changes (single nucleotide variants, small insertions and deletions), copy number variants (CNVs) for the targeted genes, and terminal copy number-neutral loss of heterozygosity (CN-LOH). This panel is a more cost-effective approach when compared to the cost of multiple single gene tests and can be used to complement the morphologic and cytogenetic workup of myeloid malignancies.

GENES TESTED: ANKRD26; ASXL1; ASXL2; BCOR; BCORL1; BRAF; CALR; CBL; CBLB; CEBPA; CSF3R; CUX1*; DDX41; DNMT1*; DNMT3A; ELANE; ETNK1; ETV6; EZH2; FBXW7; FLT3; GATA1; GATA2; GNAS; HNRNPK; IDH1; IDH2; IL7R; JAK1; JAK2; JAK3; KDM6A*; KIT; KMT2A; KRAS; LUC7L2; MPL; NOTCH1; NPM1*; NRAS; NSD1; PHF6; PIGA; PPM1D; PRPF40B; PRPF8; PTPN11; RAD21; RUNX1; SAMD9; SAMD9L; SETBP1; SF3B1; SH2B3; SMC1A; SMC3; SRSF2; STAG2; STAT3; STAT5B*; SUZ12*; TET2; TP53; U2AF1; U2AF2; UBA1; WT1; ZRSR2
*One or more exons of the preferred transcript were not covered by sequencing for the indicated gene; see limitations section below.

METHODOLOGY: Genomic DNA was isolated from peripheral blood or bone marrow and then enriched for the targeted exonic regions of the tested genes and approximately 13,000 single nucleotide polymorphisms (SNPs) evenly spaced over the coding genome. The variant status, copy number variation of the targeted genes and SNPs, and CN-LOH were determined by massively parallel sequencing. The hg19 (GRCh37) human genome assembly was used as a reference for identifying genetic variants. The following general types of variants are reported: clinically significant/uncertain sequence variants in the preferred transcript, CNVs (gains or losses) in the targeted genes, likely acquired terminal CN-LOH, and CNVs 5 megabases (Mb) or greater in size in any gene. In addition, these specific variants will also be reported: losses in additional relevant genes (ARID2, ASMTL, ATM, CD200, CDKN2A, CHEK2, ERG, IKZF1, NF1, PAX5, RB1, TBL1XR1), gains in additional relevant genes (MYC), losses between FIP1L1 and PDGFRA that result in a potential fusion, and any CN-LOH involving TP53, JAK2, and CBL.

LIMITATIONS: Variants outside the targeted regions or below the limit of detection are not identified. Variants in regions that are not included in the preferred transcript for the targeted genes are not detected. Benign or likely benign variants and likely germline or interstitial CN-LOH are not reported. In some cases, variants may not be identified due to technical limitations in the presence of pseudogenes or in repetitive or homologous regions. It is also possible some insertion/deletion variants may not be identified. RNA variants, gene fusions, translocations and other structural variants are not detected by this test. Due to complexity of analysis, CNVs may not be reported in the instance of stem cell transplants that present with mixed chimerism, increased genomic complexity (greater than four copy number variants), and complex aneuploidies (e.g., hyper- or hypodiploidy). Variant allele frequency (VAF) is not reported for CNVs with copy number greater than three. This test does not replace conventional cytogenetic studies or genomic microarray in the workup of hematologic malignancies; results from this test should be correlated with cytogenetic test

results. 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. The following regions were not sequenced due to technical limitations of the assay:
CUX1 (NM_181552) exon 24
DNMT1 (NM_001130823) exon 5
KDM6A (NM_001291415) exon 13
NPM1 (NM_002520) exon 1
STAT5B (NM_012448) exons 6-9
SUZ12 (NM_015355) exons 1-9

LIMIT OF DETECTION (LOD): 5 percent variant allele fraction (VAF) for single nucleotide variants (SNV) and small variants less than 24 base pairs (bp). Variants greater than 24 bp may be detected at LOD, but the analytical sensitivity may be reduced. LOD for CNVs is greater than 2 Mb in size in approximately 30 percent of the sample. LOD for CN-LOH is greater than 10 Mb in approximately 30 percent of the sample. Some areas of the genome may have a reduced sensitivity for CNVs and CN-LOH at LOD.

ANALYTICAL SENSITIVITY: The positive percent agreement (PPA) estimate for the respective variant classes (with 95 percent credibility region) are listed below. Genes included on this test are a subset of a larger methods-based validation from which the PPA values are derived.
Single nucleotide variants (SNVs): 96.9 percent (95.1-98.1 percent)
Insertions/duplications (1-24bp): 98.1 percent (95.5-99.3 percent)
Insertions/duplications (greater than 24bp): > 99 percent (92.9-100.0 percent)
Deletions (1-24bp): 96.7 percent (92.8-98.7 percent)
Deletions (greater than 24bp): 90 percent (79.5-96.1 percent)
Multinucleotide variants (MNVs): 97 percent (93.0-99.0 percent)
FLT3 ITDs: Greater than 99 percent (97.1-100.0 percent)
Copy number gains (greater than 2 Mb): 91.8 percent (86.7-95.3 percent)
Copy number losses (greater than 2 Mb): 92.3 percent (87.7-95.5 percent)
Copy number-neutral loss of heterozygosity (greater than 10 Mb): 98.1 percent (91.5-99.8 percent)

CLINICAL DISCLAIMER: 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 or management of malignancy. This test is not intended to detect minimal residual disease.

This test was developed and its performance characteristics determined by ARUP Laboratories. It has not been cleared or approved by the U.S. Food and Drug Administration. This test was performed in a CLIA-certified laboratory and is intended for clinical purposes.

EER Myeloid Mutation Panel NGS, DelDup

See Note

Authorized individuals can access the ARUP Enhanced Report using the following link:

[redacted]

H=High, L=Low, *=Abnormal, C=Critical

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
MYE CNV Proposed Diagnosis	23-299-108540	10/26/2023 12:22:00 PM	10/26/2023 12:22:38 PM	10/27/2023 9:01:00 AM
MYE CNV Specimen	23-299-108540	10/26/2023 12:22:00 PM	10/26/2023 12:22:38 PM	10/27/2023 9:01:00 AM
MYE CNV Interp	23-299-108540	10/26/2023 12:22:00 PM	10/26/2023 12:22:38 PM	10/27/2023 9:01:00 AM
EER Myeloid Mutation Panel NGS, DelDup	23-299-108540	10/26/2023 12:22:00 PM	10/26/2023 12:22:38 PM	10/27/2023 9:01:00 AM

END OF CHART

H=High, L=Low, *=Abnormal, C=Critical