Myeloid Malignancies Somatic Mutation and Copy Number Analysis Panel
ARUP test code 2012182

Myeloid Malignancy Proposed Diagnosis
AML unspec

Myeloid Malignancies Panel Specimen
Whole Blood

Myeloid Panel Summary
See Note
Results Summary:
I. Tier 1 variants detected by next generation sequencing (MYE NGS)
NONE DETECTED

II. Clinically significant copy number changes and long contiguous stretches of homozygosity detected by SNP microarray analysis (CMA ONC)
NONE DETECTED

Myeloid Malignancies Panel Interp
See Note
Submitted diagnosis or diagnosis under consideration for variant interpretation:
Acute myeloid leukemia, unspecified (AML, unspec)

Result:

I. Tier 1 (Variants of known significance in myeloid malignancies):
NONE DETECTED

II. Tier 2 (Variants of unknown significance in myeloid malignancies):
NONE DETECTED

Low coverage regions:
This list contains exons where the average sequencing depth (number of times a particular position is sequenced) is below our stringent cutoff of 300. The sequencing reads from these exons were manually reviewed. If high quality variants are detected in these regions they will be listed above in Tier 1 or Tier 2.
NONE

This result has been reviewed and approved by Jay Patel, M.D.

BACKGROUND INFORMATION: Myeloid Malignancies Panel Interp

CHARACTERISTICS: Myeloid malignancies are clonal disorders of hematopoietic stem and progenitor cells that include myelodysplastic syndromes (MDS), myeloproliferative neoplasms (MPN), myelodysplastic/myeloproliferative neoplasms (MDS/MPN), and acute myeloid leukemia (AML). 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 multi-gene 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 myeloid malignancies.

GENES TESTED: ANKRD26, ASXL1, ASXL2, BCR, BCR/ABL1, BRAF, CALR, CBL, CBLB, CEBPA, CSF3R, CUX1*, DDX41, DNMT1*, DNMT3A, ELANE, 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, PRPF4B, PRPF8, PTPN11, RAD21, RUNX1, SETBP1, SF3B1, SH2B3, SMCA1, SMCA3, SRSF2, STAG2, STAT3, STAT5B*, SUZ12*, TET2, TP53, U2AF1, U2AF2, 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. The variant status of the targeted genes was determined by massively parallel sequencing. The hg19 (GRCh37) human genome assembly was used as a reference for identifying genetic variants.

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. 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. The following regions were not sequenced due to technical limitations of the assay:
H=High, L=Low, *=Abnormal, C=Critical
CUX1 (NM_181552) exon 24
DNMT1 (NM_001130823) exon 5
KDM6A (NM_001291141) exon 13
NPM1 (NM_002520) exon 1
STAT5B (NM_012448) exons 6-9
SUZ12 (NM_013535) 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 24bp may be detected at LOD, but the analytical sensitivity may be reduced.

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)
Multi-nucleotide variants (MNVs): 97 percent (93.0 - 99.0 percent)
FLT3 ITDs: Greater than 99 percent (97.1 - 100.0 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 of malignancy. This test is not intended to detect minimal residual disease.

Test developed and characteristics determined by ARUP Laboratories. See compliance statement B: aruplab.com/CS

Cytogenomic Microarray SNP - Oncology

Normal

(Ref Interval: Normal)

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

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Julio C. Delgado, MD, MS, Director of Laboratories

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

Patient: Patient, Example
ARUP Accession: 20-015-111093
Patient Identifiers: 01234567890ABCD, 012345
Visit Number (FIN): 01234567890ABCD
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4848
CMA ONC TEST RESULT

Clinically significant copy number changes and long contiguous stretches of homozygosity detected by SNP microarray analysis:

NONE DETECTED

Sex chromosome complement: XX (female)

Test Information:
Chromosomal microarray analysis (CMA) was performed using Affymetrix CytoScan HD microarray. This microarray consists of 2,696,550 oligonucleotide probes across the genome, including 1,953,246 unique non-polymorphic probes, and 743,304 SNP (single nucleotide polymorphism) probes. Patient hybridization parameters are normalized to a reference set derived from 100 individuals with normal microarray results. Genomic linear positions are given relative to NCBI build 37 (hg19). Detected aberrations are reported when found to have clear or suspected clinical relevance; aberrations devoid of relevant gene content or reported as common findings in the general population may not be reported.

This microarray and associated software (Chromosome Analysis Suite) are manufactured by Affymetrix and used by ARUP Laboratories for the purpose of identifying DNA copy number gains and losses associated with large chromosomal imbalances. This analysis will not detect all forms of polyploidy, balanced rearrangements (eg. inversions and balanced chromosomal translocations), small deletions, point mutations, and some mosaic conditions. While this assay has been extensively validated by ARUP Laboratories and other clinical laboratories per ACMG guidelines, it is not feasible to validate every potential genomic imbalance in the human genome. Furthermore, this technique only identifies the regions of imbalance; it does not provide information regarding the arrangement or mechanisms responsible. For these reasons, we may recommend that some chromosomal microarray results be characterized by fluorescence in situ hybridization (FISH) or standard chromosome analysis.

The functional resolution of this assay varies across different samples dependent upon the size of the abnormality, probe density, tumor content and quality of the DNA obtained. On average, the limit of detection will vary from less than 100 kilobases for samples with high tumor content (generally greater than 70 percent) to several megabases for samples with lower tumor content (25-35 percent). The limit of detection for loss of heterozygosity (LOH) is approximately 3 megabases.

This result has been reviewed and approved by Erica F. Andersen, Ph.D., FACMG

INTERPRETIVE INFORMATION: Cytogenomic Microarray
SNP - Oncology
Test developed and characteristics determined by ARUP Laboratories. See Compliance Statement B: aruplab.com/CS
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