Myeloid Malignancies Mutation Panel by Next Generation Sequencing
ARUP test code 2011117

Myeloid Malignancies Panel Specimen  Bone Marrow

Myeloid Malignancies Panel Interp

Submitted diagnosis or diagnosis under consideration for variant interpretation:
Pancytopenia

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) for 20% or more of the region is below our stringent cutoff of 300. Sensitivity for detection of low allelic frequency mutations may be reduced in areas with low depth of coverage. 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:
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

H=High, L=Low, *=Abnormal, C=Critical
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, IGF1R, JAK1, JAK2, JAK3, KDM6A*, KIT, KMT2A, KRA, LUC7L2, MPL, NOTCH1, NPM1*, NRAS, NSD1, PHF6, PIGA, PRPF40B, PRRF8, PTPN11, RAD21, SRSF1, SETBP1, SF3B1, SH2B3, SMG6, SMG3, 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:

- 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_013353) 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. ANAYLITICAL 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 (MMVs): 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
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