

See below for Additional Technical Information topics

Myeloid Malignancies Mutation Panel by Next Generation Sequencing Cytogenomic Microarray – Oncology

Myeloid Malignancies Mutation Panel by Next Generation Sequencing

Indications for Ordering

Assess for single gene mutations, including substitutions and insertions and deletions that may have diagnostic, prognostic, and/or therapeutic significance in

- Acute myeloid leukemia
- Myelodysplastic syndromes (MDS)
- Myeloproliferative neoplasms (MPN)
- MDS/MPN overlap disorders such as chronic myelomonocytic leukemia

Test Description

Myeloid Malignancies Mutation Panel by Next Generation Sequencing

- Next generation sequencing (NGS) library construction from genomic DNA
- Enrichment for regions of interest by hybridization
- Massively parallel sequencing

Tests to Consider

Primary tests

- [Myeloid Malignancies Mutation Panel by Next Generation Sequencing 2011117](#)
- [Myeloid Malignancies Somatic Mutation and Copy Number Analysis Panel 2012182](#)

Related tests

- [CEBPA Mutation Detection 2004247](#)
- [NPM1 Mutation Detection by RT-PCR, Quantitative 3000066](#)
- [IDH1 and IDH2 Mutation Analysis, exon 4 2006444](#)
- [WT1 Mutation Detection by Sequencing 2005766](#)
- [KIT Mutations in AML by Fragment Analysis and Sequencing 2002437](#)

Disease Overview

Diagnostic issues

- Genetic targets contained in panels are relevant across the spectrum of myeloid malignancies
- Identification of one or more clonal genetic abnormalities may aid in establishing the diagnosis of a neoplasm
- Identification of certain mutations or patterns of mutations may aid in diagnostic subclassification

Prognostic and treatment issues

- Certain mutations or patterns of mutations may have prognostic significance
- Certain mutations may allow for the use of targeted therapies

Genetics

Genes – *ASXL1, ASXL2, BCOR, BCORL1, BRAF, CALR, CBL, CEBPA, CSF3R, DNMT1, DNMT3A, EED, ELANE, ETNK1, ETV6, EZH2, FAM5C, FLT3, GATA1, GATA2, HNRNPK, IDH1, IDH2, JAK2, JAK3, KDM6A, KIT, KRAS, LUC7L2, MAP2K1, MLL, MPL, NOTCH1, NPM1, NRAS, NSD1, PHF6, PRPF40B, PRPF8, PTPN11, RAD21, RUNX1, SETBP1, SF1, SF3A1, SF3B1, SMC1A, SMC3, SRSF2, STAG2, SUZ12, TET2, TP53, U2AF1, U2AF2, WT1, ZRSR2*

Mutations

A full list of targeted regions within these genes can be found at the ARUP website – [Myeloid Panel Coordinates](#) (www.aruplab.com/myeloid-panel-coordinates)

Test Interpretation

Results

- Positive – a somatic mutation in one of the 57 tested genes was detected
 - Clinical relevance (diagnosis, prognosis, therapy) will be correlated, if known
- Negative result – no mutations were detected in the sequenced genes

Limitations

- Mutations may be present below the limit of detection
- Not intended to detect minimal residual disease

Cytogenomic Microarray – Oncology

Indications for Ordering

- Preferred test at time of diagnosis for detecting prognostically important genomic abnormalities in leukemias/lymphomas and solid tumors involving
 - Loss/gain of DNA
 - Loss of heterozygosity (LOH)
- Monitor disease progression and response to therapy

Test Description

Cytogenomic Molecular Inversion Probe Array, FFPE Tissue – Oncology

- Platform – Affymetrix OncoScan
- Contains 220,000 SNP probes across the entire genome
- Average functional resolution – 20 consecutive markers

Cytogenomic SNP Microarray – Oncology

- Platform – Affymetrix CytoScan HD
- Oligo copy number and single-nucleotide polymorphism (SNP) array
- Contains >2.6 million copy number markers
- Includes 750,000 SNP probes
- Detects copy number changes and LOH
- Average marker spacing
 - Intragenic – 880 base pairs (bp)
 - Intergenic (nongene backbone) – 1,700 bp
 - Overall (gene and nongene backbone) – 1,100 bp
- Average functional resolution
 - Deletion of 25 consecutive markers
 - Duplication of 50 consecutive markers

Tests to Consider

Primary tests

- Offer whole genome coverage
- Detect copy number changes and LOH
- Differ in type of specimen and array platform

[Cytogenomic Molecular Inversion Probe Array, FFPE Tissue – Oncology 2010229](#)

- Formalin-fixed, paraffin-embedded (FFPE) tissue specimens

[Cytogenomic SNP Microarray – Oncology 2006325](#)

- Bone marrow or blood specimens

Related tests

- Fluorescence in situ hybridization (FISH) testing for specific balanced translocations may be considered, based on indication
- For a complete list of ARUP's oncology FISH tests, including probe targets and genes, see "Oncology FISH" on the [ARUP Genetics website](http://www.aruplab.com/genetics/tests/fish) (www.aruplab.com/genetics/tests/fish)

[Myeloid Malignancies Somatic Mutation and Copy Number Analysis Panel 2012182](#)

- Panel for myeloid malignancies that combines cytogenomic microarray with a next generation sequencing panel targeting genes with diagnostic, prognostic, and/or therapeutic significance

Disease Overview

Diagnostic issues

- Gains, losses, and LOH occur in malignancies – identification may be helpful for
 - Diagnosis
 - Prognosis and therapeutic decisions
 - Monitoring disease progression and response to therapy
- Conventional cytogenetic (CC) analysis for detection of genetic abnormalities in oncology is hampered by
 - Lack of tumor cell growth in cell culture
 - Subtle chromosomal abnormalities that are often missed
- FISH
 - Improved rate of detection of clonal abnormalities when compared to CC, but only for the targeted region
 - Detects balanced translocations
 - Limited because only a few loci examined at a time
- Neither conventional karyotyping nor FISH testing can detect copy-neutral events that are associated with hematological malignancies
 - Often due to mutations and subsequent selection of mutant tumor-suppressor genes and oncogenes
- SNP microarray detects many of the chromosomal variants involving gains or losses in chromosomes with complex karyotypes across the genome

Test Interpretation

Results

- Abnormal microarray
 - Well-documented and clinically significant gain or loss or LOH detected
- Copy number change detected, clinical significance unknown
 - Copy number variation detected for which insufficient evidence is available to determine unequivocally the clinical significance
- Normal microarray
 - No clinically significant abnormalities detected based on current knowledge at time of reporting

Limitations

- Low-level mosaicism (<15-20%) may not be detected
- May not be appropriate for individuals with expected lower levels of malignant cells
- FFPE specimens must contain a region with $\geq 50\%$ tumor
- Not recommended for minimal residual disease
- Does not detect
 - Balanced rearrangements
 - FISH should be used to evaluate specific balanced rearrangements according to indication
 - Base pair mutations and very small deletions/duplications
 - Imbalances of the mitochondrial genome
 - Positional information for chromosome rearrangements
 - Low-level clones