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 (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 ≥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