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<http://www.uab.edu/medicine/genetics/patient-care/clinical-labs/cytogenetics-laboratory>

Array Comparative Genomic Hybridization (array CGH) Analysis for Hematological Malignancies using the Agilent 4x180k aCGH+SNP array

The Clinical Cytogenetics Laboratory in the Department of Genetics is offering clinical array CGH testing for hematological malignancies using a whole-genome oligonucleotide (oligo) array. This test utilizes the Agilent 4x180k aCGH+SNP array, which contains ~110,000 oligo probes for the detection of genomic copy number changes, and ~60,000 SNP probes for the detection of copy-neutral loss of heterozygosity (cn-LOH). This array contains genome-wide coverage with an average probe spacing of ~25 kb. It is designed to detect copy number changes with a minimum size of ~50 kb across the genome.

Testing methodology:

Genomic DNA from the test (patient) and control samples are differentially labeled with fluorescent dyes and hybridized to the array. The competitive hybridization of the test DNA to the control DNA reveals copy number changes in the patient's DNA for the chromosomal regions tested. The array is scanned and analyzed using the "CytoGenomics v2.7" software (Agilent Technologies) to generate the final plots. This test has been validated in our laboratory using genomic DNA from patients with known hematological malignancies, including ALL, AML, MDS, CML in blast crisis, and CLL.

Interpretation and limitations:

This test will detect genomic copy number changes associated with unbalanced chromosomal rearrangements. It will detect aneuploidies, deletions, duplications, amplifications, and unbalanced translocations/insertions of the regions represented on the array, as well as cn-LOH. It has a greater resolution than both routine chromosome analysis and FISH analysis in detecting submicroscopic aberrations.

Our positive evaluation criteria include:

- Genomic DNA copy gain/loss >50 kb involving clinically significant cancer related genes (520 in the COSMIC Database).
- Genomic DNA copy loss >1 Mb or gain >2 Mb outside known clinical oncology significant regions spanning at least one annotated RefSeq gene.
- Long stretch of allele homozygosity >20 Mb on a single chromosome, which is consistent with copy-neutral loss of heterozygosity (cn-LOH). These regions suggest clonal evolution associated with the acquisition of

homozygosity for a gene mutation within the homozygotic stretch. Candidate gene(s) within these cn-LOH regions will be reported.

This test will not detect truly balanced rearrangements (reciprocal balanced translocations, Robertsonian translocations, inversions, and balanced insertions), imbalances of regions not represented on the array, low-level mosaicism, and point mutations.

Indications for testing:

1. Newly diagnosed cases with ALL, AML, MDS, and CLL.
2. CML in blast crisis.
3. Relapsed ALL and AML cases.

Specimen requirements:

1. Bone marrow (BM) aspirate in a BM transport medium tube (4-5 cc)
OR
2. Peripheral blood (PB) in one EDTA (Purple top) tube and one Na Heparin (Green top) tube (4-5 cc per tube)

At least 30% involvement of the BM or PB by the malignant process is required. Please complete the "Patient History and Request Form for Cancer Cytogenetic Analysis", which can be found at: <http://www.uab.edu/medicine/genetics/patient-care/clinical-labs/cytogenetics-laboratory>, and submit it along with the patient sample. Specimens should be transported as soon as possible at room temperature.

Turn around time:

Approximately two weeks.

CPT codes:

81229x1

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