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

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

The Clinical Cytogenetics Laboratory in the Department of Genetics is offering clinical array CGH testing using a combined targeted and whole-genome oligonucleotide (oligo) array. This test utilizes the Agilent 4x180k aCGH+SNP array, which is based on the ISCA (International Standards for Cytogenomic Arrays) Consortium design. This array contains ~110,000 oligo probes for the detection of copy number variations (CNVs), and ~60,000 SNP probes for the detection of large regions of homozygosity (i.e. absence of heterozygosity). It contains high-density coverage for ~500 targeted regions with an average oligo probe spacing of ~5 kb or at least 20 probes per gene. These targeted regions include clinically relevant haploinsufficient genes, X-linked intellectual disability genes, all recurrent microdeletion/microduplication syndrome regions, and all unique subtelomeric and pericentromeric regions. In addition, it contains genome-wide backbone coverage with an average probe spacing of ~25 kb.

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 DNA from patients with known microdeletions/microduplications, as well as unbalanced karyotypes detected by G-banded chromosome analysis.

Interpretation and limitations:

This test will detect genomic CNVs associated with unbalanced chromosomal rearrangements. It will detect aneuploidies, deletions, and duplications, as well as unbalanced translocations of the regions represented on the array. CNVs >200-300 kb will be reported. Smaller CNVs in the targeted genes/regions will also be reported. FISH or G-banded chromosome analysis will be used to confirm any clinically significant abnormality whenever possible, and the results will be interpreted using standard cytogenomic microarray nomenclature. This array will also detect large regions of homozygosity. Identification of large regions of homozygosity on a single chromosome could suggest uniparental disomy (UPD), which may warrant further clinical investigation when observed on chromosomes with known imprinting disorders associated with UPD. In addition, the detection of large regions of

homozygosity on multiple chromosomes may suggest consanguinity and, therefore, could be useful in determining candidate genes for further testing for autosomal recessive disorders. 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. The detection rate of uniparental heterodisomies is currently not known for this assay.

Indications for testing:

1. Recommended by the American College of Medical Genetics (ACMG) as a first-tier clinical diagnostic test in the initial postnatal evaluation of individuals with the following conditions:
 - Apparently non-syndromic developmental delay and/or intellectual disability
 - Autism spectrum disorders
 - Multiple congenital anomalies not specific to a well-delineated genetic syndrome
2. An appropriate follow-up test for individuals with unexplained developmental delay and/or intellectual disability, autism spectrum disorders, or congenital anomalies with a previously normal conventional chromosome study.
3. Determining the size, precise breakpoints, gene content, and any unappreciated complexity of abnormalities detected by other methods such as conventional chromosome and FISH studies.
4. Determining if apparently balanced abnormalities identified by previous conventional chromosome studies have cryptic imbalances, since a proportion of such rearrangements that appear balanced at the resolution of a chromosome study are actually unbalanced when analyzed by higher-resolution cytogenomic microarray.
5. Assessing large regions of homozygosity related to uniparental disomy or identity by descent.

Specimen requirements:

Peripheral blood in one EDTA (Purple top) tube and one Na Heparin (Green top) tube

- Adults and children: 3-4 cc per tube
- Infants: 1-2 cc per tube

Please complete the “Patient history and request form for blood 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.

Turn around time:

Approximately three to four weeks.

CPT codes:

81229x1

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