Chromosomal Microarray: CytoScan SNP Array

**Test Code:** CMSNP

**Turnaround time:** 2 weeks - 3 weeks (All abnormal findings are verbally reported immediately. Confirmatory testing for abnormalities will delay final reporting. A written preliminary report is available upon request.)

**CPT Codes:** 81229 x1

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### Condition Description

#### What is CytoScan SNP Array?

- The CytoScan SNP Array array consists of 2.6 million markers (including 750,000 SNPs) which allows for the detection of both copy number variation (CNV) and large stretches (>10 Megabases (Mb)) of absence of heterozygosity (AOH), which can result from uniparental disomy (UPD) or common descent. The design is based on recommendations from the International Standards for Cytogenomic Arrays (ISCA) Consortium (Baldwin et al. (2008) Genet Med 10(6):415-429).

#### Why Choose CytoScan?

- When compared to conventional cytogenetic testing by G-banded chromosome analysis, the CytoScan SNP array detects more than twice as many clinically significant imbalances. The literature supports offering whole genome chromosomal microarray testing as the first tier test for all genetic evaluations for developmental disabilities for developmental disabilities including birth defects, developmental delay, dysmorphic features, growth deficiency and intellectual disability (Miller et al. (2010) Am J Hum Genet 86(5):749-764; Manning and Hudgins (2010) Genet Med 12(11):742-745). Testing for chromosomal imbalances by microarray is cost effective given the greater capability to detect imbalances when compared to conventional methods. The CytoScan SNP array is roughly equivalent to the cost of chromosome analysis by G-banded analysis plus one targeted FISH study.

By combining SNP analysis with copy number detection, the CytoScan SNP Array provides one assay for the detection of genomic imbalances and UPD or homozygosity due to apparent common descent. This can help identify recessive risk alleles.

#### References


#### Indications

Chromosomal microarray is indicated for the following reasons:

- Unexplained developmental delay or intellectual disability
- Autism spectrum disorders
- Epilepsy or seizures
- Dysmorphic features, congenital anomalies or birth defects
- Normal chromosome analysis and an abnormal phenotype
- Apparently balanced chromosome rearrangements and an abnormal phenotype to look for cryptic imbalances at the breakpoints
- Characterization of a previously identified chromosome abnormality
- Suspected UPD
- Autosomal recessive condition due to suspected common ancestry

#### Methodology

DNA isolated from peripheral blood is hybridized to an array containing oligonucleotide and SNP probes across the genome to detect copy number imbalances and regions of homozygosity. FISH analysis or another method, such as G-banding, is used to confirm any abnormal findings either at the time of initial testing or upon receipt of parental samples, depending on the abnormality. Suspected UPD of chromosome 6, 7, 14 or 15 will be confirmed by methylation analysis.

#### Detection

The detection of deletions and duplications of 400 kb or greater is expected to be very high. Deletions and duplications of 400 kb or greater are reported. Smaller deletions or duplications in regions of known microdeletion/microduplication syndromes or in clinically relevant genes will also be reported. The clinical sensitivity for known microdeletion or microduplication syndromes is available in our detection rate chart. The clinical sensitivity for other disorders is dependent on the proportion of cases caused by deletions/duplications compared with other mutations not detectable by array analysis. Microarray will not detect balanced translocations, balanced inversions, imbalances smaller than the resolution of this array, point mutations or low level mosaicism (usually less than 25%) that may underlie the clinical presentation of the patient.

This test is designed to detect whole and partial chromosome UPD, multiple long stretches of absence of heterozygosity (AOH) greater than 3 Mb and AOH in clinically relevant regions. Possible UPD will be reported when a chromosome has at least one homozygous regions >10 Mb. Homozygosity due to apparent common descent will be reported when >5% of the genome is homozygous. These regions of AOH will be specified, allowing for the identification of recessive risk alleles.

#### Specimen Requirements

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Disclaimer: This information is confidential and subject to change without notice. It may not be reproduced in whole or part unless authorized in writing by an authorized EGL representative.
Submit only 1 of the following specimen types

Type: Whole Blood (EDTA and Sodium Heparin)

Specimen Requirements:
- Sodium Heparin and EDTA
- Infants (Children (>2 years)): 3-5 ml in both tubes
- Older Children & Adults: 7-10 ml in both tubes

Specimen Collection and Shipping:
Ship sample at room temperature for receipt at EGL within 24 hours of collection. Do not refrigerate or freeze.

Type: Skin Biopsy

Specimen Requirements:
- Sterile container with EGL transport media or other sterile culture media (RPMI, Hanks Solution)
- Obtain 1-2 cm pieces of tissue from a central location rather than a distal location to enhance cell viability and growth. Place in sterile container with EGL transport media or other sterile culture media. In the absence of media, place in a sterile container with a small amount of sterile saline. Use sterile dissection (no prep) for internal tissue.
- Tissue fixed in formalin cannot be used.

Specimen Collection and Shipping:
Ship sample at room temperature for receipt at EGL within 24 hours of collection. Do not refrigerate or freeze.

Type: DNA, Isolated

Specimen Requirements:
- Microtainer
- 3µg
- Isolation using the Perkin Elmer™ Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

Specimen Collection and Shipping:
Refrigerate until time of shipment in 100 ng/µL in TE buffer. Ship sample at room temperature with overnight delivery.

Special Instructions

Parental samples may be requested to interpret the clinical significance of some findings.

Sample Storage and Data Usage: As a participant in the ISCA (International Standard Cytogenomic Array) Consortium, EGL Genetics retains patient samples indefinitely for validation, educational purposes and/or research. The submitted clinical information and test results are also included in a HIPAA-compliant, de-identified public database as part of the National Institute of Health's effort to improve diagnostic testing and our understanding of the relationships between genetic changes and clinical symptoms (for information about the molecular cytogenetic database visit the consortium website at https://www.iscaconsortium.org/). Confidentiality of each sample is maintained.

Patients may request to have their samples discarded upon test completion and to opt-out of participation in the database by:
1) Checking the box provided on the test requisition or consent form
2) Calling the laboratory at (404) 778-8499 and asking to speak with a laboratory genetic counselor
3) Visiting the opt-out page: http://genetics.emory.edu/egl/opt-out

Related Tests

- STAT analysis of chromosomes 13, 18, 21, X or Y and the 22q11 region
- Targeted testing by FISH is available to family members of an individual with a deletion or duplication detected by microarray
- Prenatal Chromosomal Microarray (EmArray Cyto) (CMPRE)
- Products of Conception (POC) Microarray (EmArray Cyto) (CMPOC)
- EmArray Cyto (VA)