



Disease Information

Genomic imbalances are an underlying cause of congenital anomalies, developmental delay, mental retardation, autism, dysmorphism and numerous genetic syndromes. Routine karyotype analysis can detect some common chromosomal imbalances such as aneuploidies, but cannot detect smaller DNA rearrangements under ~4 Mb. Chromosomal Microarray Analysis (CMA) via Array-based Comparative Genomic Hybridization (aCGH) is a technique that allows for high resolution genome-wide detection of unbalanced structural and numerical chromosomal abnormalities. Importantly, the level of resolution of aCGH depends only on the size and spacing of the oligonucleotide probes on the array.

Each Ambry CMA: 105K Oligo Array (Agilent Technologies, Santa Clara CA) contains 105,000 oligonucleotide probes that cover the entire genome at a resolution of 30Kb. Probe coverage and resolution is increased in all known ~270 disease loci. A subset of 24 disease-associated genes are covered at the exon level. The array also includes probes for the pericentromeric and subtelomeric regions with dense probe coverage spanning 10 Mb at each subtelomere. In addition, there is coverage of the entire mitochondrial genome. The array detects all known microdeletion/duplication syndromes and most disorders detected by chromosomal analysis and FISH tests. This array was originally developed and validated at Baylor College of Medicine (BCM), and has been optimized over several years. Implementation of the Baylor aCGH technology at Ambry Genetics under the name of Ambry CMA: 105K Oligo Array expands the potential DNA analysis from sequencing and exon-targeted MLPA, to provide whole genome information at the discussed resolution.

aCGH detects net gain or loss of genomic material. Limits of this method are: balanced translocations, balanced insertions, inversions, point mutations, low level mosaicism, epigenetic abnormalities, uniparental disomy, or any microdeletions and duplications that are under the resolution of the array or not represented on the array may not be detected. A negative result from the analysis cannot rule out the possibility that a tested individual carries an aberration in these undetectable groups.

Testing Benefits & Indications

CMA should be considered for all individuals with syndromic or non-syndromic conditions that may be caused by genomic imbalance, including dysmorphic features, developmental delay or mental retardation, autism spectrum disorder, birth defects or other congenital anomalies. Chromosomal aberrations have been seen in 1-3% of general population with Developmental Delay. Array CGH has a much higher resolution than conventional karyotyping and many times can provide a relevant result even when the patient has an apparently normal karyotype. In addition, aCGH provides an appropriate test for patients who are candidates for multiplex or subtelomere FISH analysis. Array CGH is also clinically useful for the detection of chromosomal microdeletions/duplications in a region of interest in patients who are negative for point mutations or small intragenic aberration.

Test Description

Genomic deoxyribonucleic acid (gDNA) is isolated from the patient's specimen using a standardized kit and quantified by agarose gel electrophoresis. The aCGH method is based on the hybridization of fluorescently labeled patient genomic DNA (Cy-5) with fluorescently labeled reference DNA (Cy-3) to a 105K oligonucleotide array. Genomic patient DNA relative to the reference DNA are represented as fluorescent ratios (Cy5/Cy3) that are further quantified by image analysis software and analytical software. Quantified results indicate each targeted-DNA sequence as loss of copy number (deletion), gain of copy number (duplication) or normal copy number. This technology has been validated using patients with known microdeletions/duplications and other unbalanced karyotypes detected by traditional cytogenetic methods.

Mutation Detection Rate

The Ambry CMA: 105K Oligo array is a platform that has 105,000 probes, covering 270 disease loci and the mitochondrial genome. The backbone spacing of the probes is set at an average of 30Kb throughout the entire human genome. Probe coverage and resolution is increased at all known 270 disease regions. The CMA: 105K Oligo Array also has higher density coverage at 41 subtelomeric regions and 43 unique pericentromeric regions, and also includes 24 disease genes with individual exon coverage.

Turn-Around-Time

Chromosomal Microarray Analysis (aCGH) 7 – 14 days

Specimen Requirements

Specimen Type: Whole Blood

Volume (per tube): 4cc EDTA purple top and 4cc Sodium Heparin green top

Storage Conditions: Store at room temperature or refrigerate

Shipping Conditions: Ship via Pre-paid Ambry Chromosomal Microarray Submission Kits

CPT Codes

Chromosomal Microarray Analysis83891, 83892, 83894, 88386 , 83912

References

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