

## Result Report

<b>Ordered by</b>	Institution #: <b>03-00125</b>	<b>Customer Name: Two Ambry 2</b>
To: Vo, Timothy, MD		MRN: Age:
Ambry Genetics - Columbia		Specimen ID:
100 Columbia Bldg. 200		Specimen: <b>DNA</b>
Aliso Viejo, California 92656		Date of Birth: Collected: <b>06/01/2009</b>
Fax: 949-900-5501		Gender: Received: <b>06/01/2009</b>
		SSN: Authorized: <b>06/05/2009</b>
		Family #: <b>09-00063</b> Reported: <b>06/05/2009</b>
		Ethnicity:
		Indication: <b>Training</b>

### 105K Oligo Chromosome Microarray Analysis

#### Result:

**105K Oligo ABNORMAL LOSS**

#### Interpretation:

Abnormal Loss in copy number of 15q11.2q13.1 consistent with a diagnosis of Prader Willi Syndrome

Change	Chromosome Region	Min Interval	Min Size (Mb)	Max Size (Mb)
LOSS	chr15q11.2q13.1	20,418,329-25,950,338	5.532	7.520

arr cgh chr15q11.2q13.1(20,418,329-25,950,338)x1

Chromosomal Microarray Analysis revealed a LOSS in copy number in the long arm of chromosome 15 (15q11.2q13.1), spanning a minimum of 5.532 Mb and a maximum of 7.520 Mb. The deleted segment includes more than 20 genes and to get a complete list of genes in the above interval, input the genomic co-ordinates in any Genome Browser.

Genomic alterations of the chromosome 15q11-q13 region are associated with two distinct genomic imprinting disorders, Prader-Willi syndrome (PWS) and Angelman syndrome (AS). PWS is characterized by neonatal hypotonia, childhood obesity, hypogonadism, moderate mental retardation, and behavioral problems. The most common molecular defect found in PWS patients is a ~6-Mb chromosomal deletion of the 15q11-q13 region on the paternal chromosome. It is clear from molecular studies that PWS is primarily caused by deficiency of a paternally expressed gene or genes from the 15q11-q13 region.

Genetic counseling is a recommended option for all patients undergoing genetic testing.



Timothy Vo, PhD  
Laboratory Director

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## 105K Oligo Chromosome Microarray Analysis ASSAY INFORMATION (Supplement to Test Results)

**General 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 Ambyr 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 Ambyr Genetics under the name of Ambyr CMA: 105K Oligo Array expands the potential DNA analysis from sequencing and exon-targeted MLPA, to provide whole genome information at the discussed resolution.

**Methodology:**

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.

**Analytical Range:**

The Ambyr 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.

**Expected (Normal) Value:** Normal

**Result Reports:**

Deletions of any size covering a known disease locus are reported as an ABNORMAL LOSS and duplications of any size covering a known disease locus are report as an ABNORMAL GAIN. The copy number variant location is reported by region and location on the chromosome, and includes the min/max size (Mb) of the span of loss or gain. Parental FISH analysis may be required for interpretation of the result. Deletions less than ~100Kb and duplications less than ~300Kb outside known disease loci are not reported. Typically, Database of Genomic Variants documented deletion or duplication copy number variants (CNV) are not reported, unless there is cause to believe the CNV may be correlated with the presenting phenotype, either by uncovering a recessive mutation on the other allele, or due to some other reason. If the database information on the CNV is scarce and consists or less than one literature report, the CNV may be reported. Variants of unknown clinical significance may require follow-up of parental DNA to determine if the variant is *de novo* or to establish phase. Mitochondrial genome aberrations greater than 2Kb are recommended for referral to a mitochondrial lab for additional testing.

**Disclaimer:**

This test was developed by Baylor College of Medicine (BCM) and its performance characteristics were determined by Ambyr Genetics Corporation and BCM. The laboratory is regulated under the Clinical Laboratory Improvement Amendments 2003 as qualified to perform nonwaived testing. The Ambyr CMA: 105K Oligo Array will only detect net gain or loss of genomic material and therefore is not intended to analyze the following types of chromosomal aberrations: 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. Mitochondrial depletion is not detected. Copy number changes of less than 100kb (loss) or 300kb (gain) in regions of unknown clinical significance will not be reported. A negative result from the analysis cannot rule out the possibility that a tested individual carries an aberration in the undetectable group. Although molecular tests are highly accurate, rare diagnostic errors may occur. Possible diagnostic errors include sample mix-up, technical errors, and clerical errors. This report does not represent medical advice. Any questions, suggestions, or concerns regarding interpretation of results should be forwarded to a genetic counselor, medical geneticist, or physician skilled in interpretation of the relevant medical literature. References are available upon request.