Integrated GENETICS
LabCorp Specialty Testing Group

LabCorp
Laboratory Corporation of America

Reveal
SNP Microarray

SAMPLE REPORT

City Hospital
123 City Avenue
Anywhere, ST 12345

LCLS Specimen Number:	**123-456-7891-0**	Account Number:	12345678
Patient Name:	**Doe, Jane**	Ordering Physician:	Ordering Doctor, MD
Date of Birth:	00/00/1983	Specimen Type:	**AMNIOTIC FLUID**
Gender:	F	Date Collected:	02/01/2012
Patient ID:		Date Received:	02/02/2012
Lab Number:		CoPath Number:	
Indications:	Increased nuchal translucency; Hypothorax	Client Reference:	

Test: **Prenatal Chromosome Microarray**

Date Reported: **02/11/2012**

Genotyping Targets: 2695000

Array Type: SNP

MICROARRAY RESULT: NORMAL DOSAGE: ISODISOMY UPD 14 (SEE BELOW)

INTERPRETATION: LONG CONTIGUOUS HOMOZYGOSITY ON CHROMOSOME 14 CONSISTENT WITH ISODISOMY UPD 14

arr 14q11.2q32.33(19,281,483-106,368,585)x2 hmz

The whole genome chromosome SNP microarray (Reveal) copy number analysis was normal. No significant DNA copy number changes in the 2,695,000 region-specific SNPs (Affymetrix, Inc.) were detected within the reporting criteria indicated below.

There was, however, complete contiguous regions of allele homozygosity observed in the chromosome 14 analysis which is **strongly associated with uniparental isodisomy 14 (UPD).** There are confirmed imprinted genes on chromosome 14 which in cases of UPD 14 can result in either maternal or paternal UPD syndromes. If UPD is confirmed, there may also be residual effects of an early developmental presence of trisomy 14 during the usual rescue etiology to UPD, although no evidence of trisomy 14 was observed. Genetic counseling is recommended.

Paternal UPD 14 has been detected in 1 of 81 miscarriages with a normal karyotype (Tsukishiro et al., 2005). Clinical findings in liveborns include severe hypotonia, thoracic dystrophy, diastasis recti, swallowing difficulties with aspiration, developmental delay, and multiple minor anomalies (Stevenson DA, et al., 2004).

Maternal UPD(14) has been associated with IUGR, hypotonia at birth, feeding difficulties in early infancy, short stature, musculoskeletal findings, scoliosis, mild developmental delay, precocious puberty, and early childhood obesity (Dietz, 2003).

Microsatellite based UPD testing requiring parental blood samples is recommended for confirmation. No more DNA from the proband would be needed for the additional test.

References:

- Dietz, L.G. et al. J Med Genet 2003;40:e46
- Stevenson DA, et al. Am J Med Genet A. 2004 Sep 15;130A(1):88-91.
- Tsukishiro, S. et al. J. Hum. Genet. 50: 112-117, 2005.

*For OMIM genes listed on NCBI, please bookmark the following URL: http://1.usa.gov/pkjEDG; click on the desired chromosome number, then enter start and end linear positions in the upper and lower boxes on the left menu bar, and click "Go" for the inclusive list.

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Methodology
SNP microarray analysis was performed using the Affymetrix Cytoscan HD platform which uses over 743,000 SNP probes and 1,953,000 NPCN probes with a median spacing of 0.88 kb. 250ng of total genomic DNA extracted from lymphocytes was digested with NspI and then ligated to NspI adaptors, respectively, and amplified using Titanium Taq with a GeneAmp PCR System 9700. PCR products were purified using AMPure beads and quantified using NanoDrop 8000. Purified DNA was fragmented and biotin labeled and hybridized to the Affymetrix Cytoscan HD GeneChip. Data was analyzed using Chromosome Analysis Suite. **The analysis is based on human genome version GRCh37/hg19.**

Positive evaluation criteria include:
- Copy numbers gains >2Mb and losses >1Mb, including at least one OMIM annotated gene are reported in this analysis.
- Gains/losses of >50 Kb within custom clinically significant gene set. On request candidate genes can be analyzed at a much lower threshold, depending on gene specific marker density.
- UPD testing is recommended for patient results demonstrating a long contiguous region of homozygosity in a single chromosome of >20 Mb interstitially or >10 Mb telomerically (15 and 8 Mb, respectively, for imprinted chromosomes).
- Contiguous homozygosity of >8Mb within multiple chromosomes suggests common descent. These regions of potential recessive allele risk are designated prenatally only when the total is consistent with first cousin parentage or greater.
- Triploid DNA that normalizes to 2 copies in standard CGH array analysis, are detectable in this allele specific microarray by 2:1 allele dosage ratios generated within each chromosome. Complete moles are accurately detected by the presence of whole genome allele homozygosity.

Truly balanced chromosome alterations will not be detected by this analysis, although cryptic imabalance associated with some translocations are readily detected due to the dense whole genome probe coverage. The threshold for mosaicism is variable, depending on the size of segment. Empiric studies have detected whole chromosome 22 mosaicism below 10.0%. CNVs cited in the Database of Genomic Variants are not reported.

This test was developed and its performance characteristics determined by Laboratory Corporation of America Holdings (LabCorp). It has not been cleared or approved by the Food and Drug Administration(FDA). The FDA has determined that such clearance or approval is not necessary.

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Board Certified Cytogeneticist

Test Site: LabCorp
1904 Alexander Drive, RTP, NC 27709-0153 (800) 533-0567