Integrated GENETICS
LabCorp Specialty Testing Group

Reveal™ SNP Microarray

**Client/Sending Facility:**
LABCORP OF AMERICA
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1912 ALEXANDER DR
RTP, NC 27709
Ph: (919)361-7700
Fax: (919) 361-7296 NCB-13

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|---|---|---|---|
| **LCLS Specimen Number:** | **106-225-9015-0** | Account Number: | 90001555 |
| Patient Name: | **REPORT, SAMPLE** | Ordering Physician: | |
| Date of Birth: | 06/12/1989 | Specimen Type: | **AMNIOTIC FLUID** |
| Gender: | F | Client Reference: | |
| Patient ID: | | Date Collected: | 04/15/2024 |
| Lab Number: | YU24-40011 GA | Date Received: | 04/15/2024 |
| Indications: | | Date Reported: | **05/17/2024** |

Test: **Chromosome Amnio RFX CMA**

| | | | |
|---|---|---|---|
| Cells Counted: | 15 | Cells Karyotyped: | 2 |
| Colonies Counted: | 15 | Band Resolution: | 450 |
| Cells Analyzed: | 15 | | |

**CYTOGENETIC RESULT: 46,XX**

**INTERPRETATION: NORMAL FEMALE KARYOTYPE**

Cytogenetic analysis of cultured amniocytes has revealed a FEMALE karyotype with an apparently normal GTG banding pattern in all in-situ colonies or subcultured metaphases analyzed.

This result does not exclude the possibility of subtle rearrangements below the resolution of cytogenetics or congenital anomalies due to other etiologies.

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| Test: | **Chromosome Microarray** | | |
| Genotyping Targets: | 2772571 | Array Type: | SNP |

**MICROARRAY RESULT: 1.4 MB INTERSTITIAL DELETION OF 17Q12->Q12**

**INTERPRETATION: FEMALE WITH 17Q12 MICRODELETION**

**arr[hg19] 17q12(34,815,072-36,215,917)x1**

The whole genome SNP microarray (Reveal) analysis revealed a female with an interstitial deletion of the chromosomal segment listed above. This interval includes numerous OMIM genes (start: *ZNHIT3* to end: *HNF1B)*. The region is flanked by segmental duplications which predisposes to unequal meiotic recombination, resulting in both deletions and duplications.

Deletion of this region that includes the *HNF1B* gene (OMIM:189907) is associated with a variable phenotype that may include one or more of the following: cystic renal disease, pancreatic atrophy, liver abnormalities, cognitive impairment and structural brain abnormalities, diabetes (maturity-onset) and epilepsy (see references). Prenatal cases have also been reported with ultrasound abnormalities such as cystic kidney, poly/oligohydramnios and diaphragmatic hernia (see references; Hendrix; Chen). *Due to the variability of this disorder, precise prenatal prediction of a phenotype is not possible.*

Parental follow-up analysis is recommended to determine whether this deletion represents an inherited or de novo change.

No other DNA copy number changes or copy neutral ROH were detected within the present reporting criteria. **Genetic counseling is recommended.**

The follow-up parental blood (green top sodium heparin) should be submitted under test code **511810 (qPCR)**. **There is no charge for qPCR follow-up studies to prenatal arrays.** If parental studies are negative, consistent with a de novo CNV, parental FISH may be considered to rule out a rare balanced rearrangement. Parental follow-up for de novo CNVs is available at a charge and may take up to 56 days for results. Please reference the prenatal specimen number when submitting parental or familial samples. Billing policy details are available for view on www.labcorp.com.

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Maternal cell contamination studies will be reported under separate cover, if ordered.

**References:**

Mitchel MW, Moreno-De-Luca D, Myers SM, et al. 17q12 Recurrent Deletion Syndrome. 2016 Dec 8 [Updated 2020 Oct 15]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2022. Available from: https://www.ncbi.nlm.nih.gov/books/NBK401562/

George AM, et al. Recurrent Transmission of a 17q12 Microdeletion and a Variable Clinical Spectrum. Mol Syndromol. 2012 Jan;2(2):72-75. PMID: 22511894

Nik-Zainal S, et al. High incidence of recurrent copy number variants in patients with isolated and syndromic Müllerian aplasia. J Med Genet. 2011 Mar;48(3):197-204. PMID: 21278390

Moreno-De-Luca D, et al. Deletion 17q12 is a recurrent copy number variant that confers high risk of autism and schizophrenia. Am J Hum Genet. 2010 Nov 12;87(5):618-30. PMID: 21055719

Nagamani SC, et al. Clinical spectrum associated with recurrent genomic rearrangements in chromosome 17q12. Eur J Hum Genet. 2010 Mar;18(3):278-84. PMID: 19844256

Goumy C, et al. Congenital diaphragmatic hernia may be associated with 17q12 microdeletion syndrome. Am J Med Genet A. 2015 Jan;167A(1):250-3. PMID: 25425496.

Hendrix NW, et al. Prenatally diagnosed 17q12 microdeletion syndrome with a novel association with congenital diaphragmatic hernia. Fetal Diagn Ther. 2012;31(2):129-33. PMID: 22178801.

Chen CP, et al. Detection of recurrent transmission of 17q12 microdeletion by array comparative genomic hybridization in a fetus with prenatally diagnosed hydronephrosis, hydroureter, and multicystic kidney, and variable clinical spectrum in the family. Taiwan J Obstet Gynecol. 2013 Dec;52(4):551-7. PMID: 24411042.

**Methodology:**

SNP microarray analysis was performed using the Cytoscan ® HD Accel platform which uses 2,029,441 nonpolymorphic copy number probes and 743,130 SNP probes for LOH/AOH analysis and relationship assessment. The array has an average intragenic spacing of 0.818 kb and average intergenic spacing of 1.51 kb. Total genomic DNA was extracted from the sample type provided, digested with Xce1, and then ligated to Xce1 adaptors. PCR products were purified and quantified. Purified DNA was fragmented, biotin labeled, and hybridized to the Cytoscan ® HD Accel Gene Chip. Data were analyzed using Chromosome Analysis Suite. The analysis is based on the GRCh37/hg19 assembly. This test was developed

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and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug administration.
Positive evaluation criteria include:
* DNA copy number loss of >1 Mb or gain >2 Mb outside known clinically significant regions with at least one OMIM gene.
* DNA copy gain/loss within or including a known clinically significant gene of 25 kb or greater.
* 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 >8 Mb within multiple chromosomes suggests common descent. These regions of potential recessive allele risk are designated.
* A high level of allele homozygosity due to numerous contiguous short runs (associated with a geographically or socially limited gene pool) is reported at the 99th percentile.
* Triploid DNA normalizes to 2 copies in array analysis, but is detectable in this allele specific SNP microarray by the characteristic 2:1 allele ratios and pattern generated within each autosome.

SNP chromosomal microarray cannot detect:
* Truly balanced chromosome alterations
* Sequence variants
* Small insertions and deletions (indels)
* Changes in regions not represented by probes on the array
* Tetraploidy
* Low level mosaicism
* Whole chromosome uniparental heterodisomy without parental specimens
* Imbalances in the mitochondrial genome

Single gene partial or intragenic copy number variants (CNVs) detected by an independent technology such as next generation sequencing (NGS) may not be detectable by microarray. The ability to detect the CNV is dependent on size and probe coverage. The threshold for mosaicism is variable, depending on the size of the segment and array quality. Empiric studies have detected mosaicism for trisomy of a whole autosome below 10.0%. CNVs that are known to be common in the population may not be reported.

Gloria Haskell

GLORIA HASKELL, PHD, FACMG

Anjen Chenn, M.D., Ph.D.
Medical Director

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