Integrated GENETICS
LabCorp Specialty Testing Group

Reveal SNP Microarray

Client/Sending Facility:
LABCORP OF AMERICA
CMBP
1912 ALEXANDER DR
RTP, NC 27709
Ph: (919)361-7700
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LCLS Specimen Number:	**106-225-9014-0**	Account Number:	90001555
Patient Name:	**REPORT, SAMPLE**	Ordering Physician:	
Date of Birth:	05/16/1994	Specimen Type:	**AMNIOTIC FLUID**
Gender:	F	Client Reference:	
Patient ID:		Date Collected:	04/15/2024
Lab Number:	YU24-40010 GM	Date Received:	04/15/2024
Indications:		Date Reported:	**05/17/2024**
Test:	**Chromosome Microarray**		
Genotyping Targets:	2772571	Array Type:	SNP

MICROARRAY RESULT: 3.64 MB INTERSTITIAL DELETION OF 17P11.2->P11.2

INTERPRETATION: FEMALE WITH SMITH-MAGENIS SYNDROME

arr[hg19] 17p11.2(16,772,264-20,413,433)x1

The whole genome SNP microarray (Reveal) analysis has identified a female with an interstitial deletion of the chromosome segment listed above. The deleted region includes numerous OMIM genes (start: *TNFRSF13B* to end: *SPECC1)*, including *RAI1*, the primary gene implicated in Smith-Magenis syndrome. Smith-Magenis syndrome is characterized by distinctive physical features, developmental delay, cognitive impairment, and behavioral abnormalities (see reference).

Parental FISH follow-up analysis is recommended to confirm a *de novo* origin and rule out a balanced rearrangement with high recurrence risk.

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 **511770 (FISH)**. **Charges will apply.** Please reference the proband name, date of birth, and specimen number when submitting parental or familial samples. Billing policy details are available for view on www.labcorp.com.

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

Reference:

Smith ACM, Boyd KE, Brennan C, et al. Smith-Magenis Syndrome. 2001 Oct 22 [Updated 2022 Mar 10]. 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/NBK1310/

Methodology:

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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 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.

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Test: **FISH Amnio Rfx CMA or Chromo**

Cells Counted: 50 Cells Analyzed: 50

FISH RESULT: FEMALE WITH NO NUMERICAL ABNORMALITY FOR CHROMOSOMES X, 13, 18, AND 21

INTERPRETATION: NORMAL RESULT

nuc ish Xcen(DXZ1x2),Ycen(DYZ3x0),18cen(D18Z1x2),
13q14(RB1x2),21q22.12(RCAN1x2)

Fluorescence in situ hybridization (FISH) analysis of uncultured amniocytes revealed two hybridization signals for chromosomes X, 13, 18, and 21. These results are consistent with a female fetus with no aneuploidy for chromosomes X, 13, 18, or 21.

Clinical decisions should not be based solely on prenatal FISH testing. Results should be interpreted within the context of a full cytogenetic analysis, ultrasound findings, and any additional prenatal testing. Genetic counseling is recommended.

Threshold:
Fewer than 10% of interphase cells with three signals is considered background while greater than 60% is consistent with full trisomy. A minimum of 50 cells/probe is required for a full analysis. Less than a 50 cell count reduces the sensitivity of the study.

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 U.S. Food and Drug Administration. The DNA probe vendor for this study was Kreatech (Leica BioSystems), and Applied Spectral Imaging (ASI) system was used for digital image analysis.

Reference:
American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Obstetrics; Committee on Genetics; Society for Maternal–Fetal Medicine. Practice Bulletin No. 162: Prenatal Diagnostic Testing for Genetic Disorders. Obstet Gynecol. 2016 May;127(5):e108-22. PMID: 26938573.

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Gloria Haskell

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