ARUP LABORATORIES | aruplab.com
500 Chipeta Way, Salt Lake City, Utah 84108-1221
phone: 801-583-2787, toll free: 800-522-2787
Tracy I. George, MD, Chief Medical Officer

Patient Report

Patient Age/Sex: Male

Specimen Collected: 20-Dec-21 09:49

Cytogenomic SNP Microarray - Fetal	**|Received: 20-Dec-21 09:49**		**Report/Verified: 21-Dec-21 09:00**
Procedure	**Result**	**Units**	**Reference Interval**
Maternal Contamination Study Fetal Spec	Unknown Origin [f1]		
Maternal Specimen	No		

Cytogenomic SNP Microarray - Fetal	**|Received: 21-Dec-21 09:00**		**Report/Verified: 21-Dec-21 09:07**
Procedure	**Result**	**Units**	**Reference Interval**
Cytogenomic SNP Microarray -Fetal	See Note [f2 i1]		Normal

Result Footnote

f1: Maternal Contamination Study Fetal Spec

Single genotype. A maternal specimen was not submitted for correlation. The fetal sample was tested using STR markers to rule out maternal cell contamination. Only a single genotype was detected. Testing a maternal sample can confirm that this genotype is from the fetus.

This result has been reviewed and approved by Rong Mao, M.D.

f2: Cytogenomic SNP Microarray - Fetal
Test Performed: Cytogenomic SNP Microarray- Fetal (ARRAY FE)
Specimen Type: Direct (uncultured) amniocytes
Indication for Testing: NIPT inconclusive SCA

RESULT SUMMARY
Copy Number Variant Detected- Recessive Disease Risk (Female)

2q13 Deletion (Including NPHP1)

Classification: Autosomal Recessive Disease Risk
Copy number change: 2q13 loss
Size: 110 kb

RESULT DESCRIPTION
This analysis showed an interstitial deletion (1 copy present) involving chromosome 2 within 2q13. This region contains the following 3 genes: MALL, NPHP1, and MTLN.

This is a deletion of the 2q13 (NPHP1) region, with recurrent breakpoints (BPs) within flanking low-copy repeat regions. The reported size of this deletion may vary across studies due to variability in breakpoints within flanking repeat regions.

INTERPRETATION
The clinical significance of this finding is uncertain and may be unrelated to the indication for testing. Deletions and other pathogenic variants affecting both copies of the gene NPHP1 are associated with autosomal recessive familial juvenile nephronophthisis (OMIM 256100) and Joubert syndrome 4 (OMIM 609583). This finding is reported due to an accompanying recessive disease risk.

The heterozygous deletion identified is a pathogenic variant of one of the two alleles. While not diagnostic, it indicates this fetus is at least a carrier for this disorder. Other genes in this interval are not known to be associated with congenital anomalies or neurocognitive deficits when deleted. Of note, similar deletions have been observed in numerous individuals from studies of natural genomic variation, and therefore, are common in the general population.

*=Abnormal, #=Corrected, C=Critical, f=Result Footnote, H-High, i-Test Information, L-Low, t-Interpretive Text, @=Performing lab

Result Footnote

f2: Cytogenomic SNP Microarray - Fetal

Correlation of the fetal phenotype with the clinical features of these recessive conditions may be considered. If indicated, molecular testing may be warranted, as microarray technology cannot identify all types of pathogenic variants.

Recommendations:
1) Genetic counseling, as this deletion may be inherited from a parent
2) Clinical correlation with features of the recessive conditions above, as indicated

Health care providers with questions may contact an ARUP genetic counselor at (800) 242-2787 ext. 2141.

References:
1) Brancati et al. Joubert Syndrome and related disorders. Orphanet J Rare Dis. 2010 Jul 8;5:20. PMID: 20615230.
2) Parisi. Clinical and molecular features of Joubert syndrome and related disorders. Am J Med Genet C Semin Med Genet. 2009 Nov 15;151C(4):326-40. PMID: 19876931.
3) Salomon et al. Nephronophthisis. Pediatr Nephrol. 2009 Dec;24(12):2333-44. PMID: 18607645.

Cytogenomic Nomenclature (ISCN):
arr[GRCh37] 2q13(110873835_110983418)x1

Technical Information
- This assay was performed using the CytoScan™ HD Suite (Thermo Fisher Scientific) according to validated protocols within the Genomic Microarray Laboratory at ARUP Laboratories
- This assay is designed to detect alterations to DNA copy number state (gains and losses), copy-neutral alterations (regions of homozygosity; ROH) that indicate an absence- or loss-of-heterozygosity (AOH or LOH), and certain alterations to ploidy state due to errors at fertilization or early embryonic cell division (i.e. triploidy, molar pregnancy)
- AOH may be present due to molar pregnancy, parental relatedness (consanguinity) or uniparental disomy (UPD)
- LOH may be present due to acquired UPD (segmental or whole chromosome)
- The detection sensitivity (resolution) for any particular genomic region may vary dependent upon the number of probes (markers), probe spacing, and thresholds for copy number and ROH determination
- The CytoScan HD array contains 2.67 million markers across the genome with average probe spacing of 1.15 kb, including 750,000 SNP probes and 1.9 million non-polymorphic probes
- In general, the genome-wide resolution is approximately 25-50 kb for copy number changes and approximately 3 Mb for ROH (See reporting criteria)
- The limit of detection for mosaicism varies dependent upon the size and type of genomic imbalance. In general, genotype mixture due to mosaicism (distinct cell lines from the same individual) or chimerism (cell lines from different individuals) will be detected when present at greater than 20-30 percent in the sample
- Genomic coordinates correspond to the Genome Reference Consortium human genome build 37/human genome issue 19 (GRCh37/hg19)

Variant Classification and Reporting Criteria
- Copy number variant (CNV) analysis is performed in accordance with recommendations by the American College of Medical Genetics and Genomics (ACMG), using standard 5-tier CNV classification terminology: pathogenic, likely pathogenic, variant of uncertain significance (VUS), likely benign, and benign
- CNVs classified as pathogenic or likely pathogenic are generally reported based on information available at the time of review
- CNVs classified as VUS are generally reported when found to have suspected clinical relevance based on information available at the time of review, or when meeting size criteria
- Known or expected pathogenic CNVs affecting genes with known clinical significance but which are unrelated to the indication for testing will generally be reported

Result Footnote

f2: Cytogenomic SNP Microarray - Fetal
- Variants that do not fall within the standard 5-tier CNV classification categories may be reported with descriptive language specific to that variant
- In general, recessive disease risk and recurrent CNVs with established reduced penetrance will be reported
- For a list of databases used in CNV classification, please refer to ARUP Constitutional CNV Assertion Criteria, which can be found on ARUP's Genetics website at www.aruplab.com/genetics
- CNVs classified as likely benign or benign that are devoid of relevant gene content or reported as common findings in the general population, are generally not reported
- CNV reporting (size) criteria: losses greater than 1 Mb and gains greater than 2 Mb are generally reported, dependent on genomic content
- Regions of homozygosity (ROH) are generally reported when a single terminal ROH is greater than 3 Mb and a single interstitial ROH is greater than 10-20 Mb (dependent upon chromosomal location and likelihood of imprinting disorder) or when total autosomal homozygosity is greater than 5 percent (only autosomal ROH greater than 3 Mb are considered for this estimate)

Limitations
This analysis cannot provide structural (positional) information associated with genomic imbalance. Therefore, additional cytogenetic testing by chromosome analysis or fluorescence in situ hybridization (FISH) may be recommended.

Certain genomic alterations may not or cannot be detected by this technology. These alterations may include, but are not limited to:
- CNVs below the limit of resolution of this platform
- Sequence-level variants (mutations) including point mutations and indels
- Low-level mosaicism (generally, less than 20-30 percent)
- Balanced chromosomal rearrangements (translocations, inversions and insertions)
- Genomic imbalance in repetitive DNA regions (centromeres, telomeres, segmental duplications, and acrocentric chromosome short arms)
- Most cases of tetraploidy

This result has been reviewed and approved by Cinthya J. Zepeda Mendoza, PhD

Test Information

i1: Cytogenomic SNP Microarray - Fetal

INTERPRETIVE INFORMATION: Cytogenomic SNP Microarray - Fetal

This test was developed and its performance characteristics determined by ARUP Laboratories. It has not been cleared or approved by the US Food and Drug Administration. This test was performed in a CLIA certified laboratory and is intended for clinical purposes.

Counseling and informed consent are recommended for genetic testing. Consent forms are available online.