ARUP LABORATORIES
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Tracy I. George, MD, Chief Medical Officer

Client: Example Client ABC123
123 Test Drive
Salt Lake City, UT 84108
UNITED STATES

Physician: Doctor, Example

Patient: Patient, Example

DOB	7/21/1992
Gender:	Female
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	01/01/2017 12:34

Cytogenomic Molecular Inversion Probe Array, FFPE Tissue - Products of Conception

ARUP test code 2010795

Cytogenomic MIP Array FFPE, POC

Abnormal * (Ref Interval: Normal)

Test Performed: Cytogenomic Molecular Inversion Probe Array, FFPE Tissue- Products of Conception (CMA PFFPE)
Specimen Type: Products of Conception (Villi)
Estimated Villi/Fetal Content: 90 percent
Indication for Testing: Products of Conception

RESULT SUMMARY
Abnormal Microarray Result (Male)

Trisomy 13

Classification: Pathogenic
Copy number change: 13q11q34 gain
Size: 95.7 Mb

RESULT DESCRIPTION
This analysis showed a gain of all probes on chromosome 13, indicating an additional copy (trisomy) of this chromosome.

INTERPRETATION
This result is consistent with a diagnosis of trisomy 13, which has a reported fetal loss rate of approximately 50 percent between 10-13 weeks gestation and term. Features associated with trisomy 13 in the prenatal period may include heart defects, holoprosencephaly, cleft lip with or without cleft palate, renal malformations, intrauterine growth restriction, polydactyly, clenched fists, and rocker-bottom feet.

Autosomal trisomy is the most frequent type of chromosomal abnormality in pregnancy loss and is usually sporadic.

NOTE: Genomic microarray analysis cannot provide structural information accounting for this gain. As it is uncertain whether this finding represents three independent copies of chromosome 13 or may be due to an unbalanced Robertsonian translocation, parental chromosome analysis should be considered to determine carrier status and to assess recurrence risk.

Recommendations:
1) Genetic counseling
2) Parental chromosome analysis. This test is available, at a charge, through ARUP Laboratories. Please order test code 2002289 Chromosome Analysis, Peripheral Blood and include the name/DOB of the proband.

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

H=High, L=Low, *=Abnormal, C=Critical

References:
1) Pont et al. Congenital malformations among liveborn infants with trisomies 18 and 13. Am J Med Genet A. 2006 Aug 15;140(16):1749-56. PMID: 16835915.
2) Morris and Savva. The risk of fetal loss following a prenatal diagnosis of trisomy 13 or trisomy 18. Am J Med Genet A. 2008 Apr 1;146A(7):827-32. PMID: 18361449.
3) Gardner and Amor. Robertsonian Translocations. In: Gardner and Sutherlands Chromosome Abnormalities and Genetic Counseling. 5th edition. New York, NY: Oxford; 2018:142-157.
4) Milunsky. Chapter 4: Prenatal Diagnosis of Chromosomal Abnormalities through Chorionic Villus Sampling and Amniocentesis. In: Milunsky and Milunsky, eds. Genetic Disorders and the Fetus. 7th edition. West Sussex, UK: John Wiley and Sons; 2016:178-266.

Cytogenetic Nomenclature (ISCN):
arr(13)x3

Technical Information
- This assay was performed using the OncoScan(TM) CNV Assay (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) as well as 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 OncoScan CNV array contains over 220,000 SNP probes with a median probe density (kb/probe) of 16-19 kb
- In general, the genome-wide resolution is approximately 300-400 kb for copy number changes and approximately 5 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, likely pathogenic or variant of uncertain significance, are generally reported, based on information available at the time of review
- Known or expected pathogenic CNVs affecting genes with known clinical significance but which are unrelated to the indication for testing will generally be reported
- 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 ARUPs 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 and gains greater than 500 kb are generally reported, dependent on genomic content
- ROH are generally reported when a single terminal ROH is greater than 5 Mb and a single interstitial ROH is greater than 10-15 Mb (dependent upon chromosomal location and likelihood of imprinting disorder) or when total autosomal homozygosity is greater than 3 percent (only autosomal ROH greater than 5 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 [redacted]

INTERPRETIVE INFORMATION: Cytogenomic Molecular Inversion Probe Array, FFPE Tissue - Products of Conception

Test developed and characteristics determined by ARUP Laboratories. See Compliance Statement C: aruplab.com/CS

EER Cytogenomic MIP Array FFPE, POC	EERUnavailable
Block ID	SX20-248 A3

H=High, L=Low, *=Abnormal, C=Critical

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
Cytogenomic MIP Array FFPE, POC	20-100-400883	3/27/2020 1:03:00 PM	4/10/2020 12:49:39 PM	4/25/2020 6:22:00 PM
EER Cytogenomic MIP Array FFPE, POC	20-100-400883	3/27/2020 1:03:00 PM	4/10/2020 12:49:39 PM	4/25/2020 6:22:00 PM
Block ID	20-100-400883	3/27/2020 1:03:00 PM	4/10/2020 12:49:39 PM	4/10/2020 2:50:00 PM

END OF CHART

H=High, L=Low, *=Abnormal, C=Critical