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

Physician: Doctor, Example

## Patient: Patient, Example

| | |
|---|---|
| **DOB** | 8/15/1988 |
| **Gender:** | Female |
| **Patient Identifiers:** | 01234567890ABCD, 012345 |
| **Visit Number (FIN):** | 01234567890ABCD |
| **Collection Date:** | 00/00/0000 00:00 |

## Genomic SNP Microarray, Products of Conception

ARUP test code 2005633

SNP Microarray, Products of Conception

**Abnormal** * **(Ref Interval: Normal)**

Test Performed: Genomic SNP Microarray, Products of Conception (ARRAY POC)
Specimen Type: Products of Conception (Tissue: Fetal)
Indication for Testing: Fetal demise

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RESULT SUMMARY
Abnormal Microarray Result (Female)

Trisomy 21 (Down syndrome)

Classification: Pathogenic
Copy number change: 21q11.2q22.3 gain
Size: 33.1 Mb

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RESULT DESCRIPTION
This analysis showed a gain of all probes on chromosome 21, indicating an additional copy (trisomy) of this chromosome.

INTERPRETATION
This result is consistent with a diagnosis of trisomy 21 (Down syndrome), which has a reported fetal loss rate of approximately 40 percent between 10-13 weeks gestation and term. Features associated with trisomy 21 in the prenatal period may include anomalies involving the heart and diaphragm, as well as nuchal thickening, cystic hygroma, echogenic bowel and shortened femur.

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 21 or an unbalanced Robertsonian translocation, follow-up testing should be considered (see recommendations).

Recommendations:
1) Genetic counseling
2) Chromosome analysis. For assistance with ordering testing on this sample, please call ARUP Genetics Processing at (800) 242-2787 ext. 3301 and refer to test code 2002288, Chromosome Analysis, Products of Conception within 7 days.
3) If chromosome analysis on the products of conception sample is not possible, parental chromosome analysis may be considered to determine carrier status for recurrence risk counseling. This test is available, at a charge, through ARUP Laboratories. Please order test code 2002289, Chromosome Analysis, Peripheral Blood and include the accession number for this case.]

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

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

References:
1) Sheets et al. Practice guidelines for communicating a prenatal or postnatal diagnosis of Down syndrome: recommendations of the national society of genetic counselors. J Genet Couns. 2011 Oct;20(5):432-41. PMID: 21618060.
2) Morris et al. Fetal loss in Down syndrome pregnancies. Prenat Diagn. 1999 Feb;19(2):142-5. PMID: 10215072.
3) Gardner and Amor. Gardner and Sutherlands Chromosome Abnormalities and Genetic Counseling. 5th edition. New York, NY: Oxford; 2018: 142-157 and 229-255.
5) Milunsky. Genetic Disorders and the Fetus: Diagnosis, Prevention and Treatment. 7th edition. West Sussex, UK: John Wiley and Sons; 2016:178-266.

Cytogenetic Nomenclature (ISCN):
arr(21)x3

Technical Information
- This assay was performed using the CytoScan(TM) 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) 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 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, 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 greater than 50 kb and gains greater than 400 kb are generally reported, dependent on genomic content
- ROH are generally reported when a single terminal ROH is greater than 3 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 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

INTERPRETIVE DATA: Genomic SNP Microarray,
Products of Conception
Test developed and characteristics determined by ARUP Laboratories. See Compliance Statement C: aruplab.com/CS

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|---|---|
| EER SNP Microarray, Products of Concept | EERUnavailable |

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

VERIFIED/REPORTED DATES

| Procedure | Accession | Collected | Received | Verified/Reported |
|---|---|---|---|---|
| SNP Microarray, Products of Conception | 20-206-400069 | 00/00/0000 00:00 | 00/00/0000 00:00 | 00/00/0000 00:00 |
| EER SNP Microarray, Products of Concept | 20-206-400069 | 00/00/0000 00:00 | 00/00/0000 00:00 | 00/00/0000 00:00 |

END OF CHART

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