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

Physician: Doctor, Example

Patient: Patient, Example

DOB	3/3/1988
Gender:	Female
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	00/00/0000 00:00

Cytogenomic SNP Microarray - Fetal

ARUP test code 2002366

Maternal Contamination Study Fetal Spec	Fetal Cells Single fetal genotype present; no maternal cells present. Fetal and maternal samples were tested using STR markers to rule out maternal cell contamination. This result has been reviewed and approved by [redacted]
Maternal Specimen	Yes
Cytogenomic SNP Microarray - Fetal	**Abnormal** * **(Ref Interval: Normal)** Test Performed: Cytogenomic SNP Microarray- Fetal (ARRAY FE) Specimen Type: Direct (uncultured) amniocytes Indication for Testing: Maternal Xq28 terminal deletion identified (ARUP accession 23-146-133397) after atypical cfDNA screening result --- RESULT SUMMARY Abnormal Microarray Result (Female) 1) Xq28 Terminal Deletion Classification: Pathogenic Copy number change: Xq28 loss Size: 4.9 Mb Copy Number Variant Detected- Recessive Disease Risk 2) 16p13.2 Deletion Classification: Autosomal Recessive Disease Risk Copy number change: 16p13.2 loss Size: 23 kb --- RESULT DESCRIPTION This analysis showed a terminal deletion (1 copy present) involving the X chromosome within Xq28. This region contains at least 130 genes (listed below). NOTE: This result indicates that this individual is a carrier of the maternal Xq28 deletion.

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

This analysis also showed an interstitial deletion (1 copy present) involving chromosome 16 within 16p13.2. This region is intragenic within the gene PMM2 (minimally exons 4-7 of 8 total exons; RefSeq NM_000303.3). This deletion removes a significant portion of this gene and is predicted to result in a loss-of-function for one copy of this gene.

INTERPRETATION

1) Xq28 Deletion

Due to the large size and number of genes involved, this deletion is expected to be clinically significant. Deletions involving this particular region of Xq28 are rare in the literature, although a number of female patients with overlapping deletions have been reported. Clinical features are variable and may include developmental delay/intellectual disability, hypotonia, craniofacial dysmorphism, amenorrhea, and infertility (including primary ovarian failure). Clinical correlation should be performed with careful consideration, as the size of the deletions reported in the literature may vary significantly from that reported here.

The effects of aberrations on the X chromosome in females may be moderated by X-inactivation. Therefore, female carriers of pathogenic X chromosome variants may be clinically unaffected, mildly affected, or, in some cases, affected similarly to males.

Based on previous parental testing, this deletion is maternally inherited. Additionally, this fetus is at risk to have affected offspring.

2) 16p13.2 Deletion

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 PMM2 are associated with autosomal recessive congenital disorder of glycosylation type Ia (OMIM 212065). 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.

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

Recommendations:
1) Genetic counseling
2) Clinical correlation with features of the recessive condition above, as indicated

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

References:
1) Mercer et al. Detailed clinical and molecular study of 20 females with Xq deletions with special reference to menstruation and fertility. Eur J Med Genet. 2013 Jan;56(1):1-6. PMID: 23059468.
2) Marshall et al. Deletion Xq27.3q28 in female patient with global developmental delays and skewed X-inactivation. BMC Med Genet. 2013 May 1;14:49. PMID: 23634718.

Cytogenomic Nomenclature (ISCN):
arr[GRCh37]
Xq28(150351569_155233731)x1mat,16p13.2(8899461_8922426)x1

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Genes within the Xq28 deleted region:
VMA21, LOC105377213, PASD1, PRRG3, FATE1, CNGA2, MAGEA4-AS1, MAGEA4, GABRE, MIR224, MIR452, MAGEA5, MAGEA10-MAGEA5, MAGEA10, GABRA3, MIR105-1, MIR767, MIR105-2, GABRQ, MAGEA6, CSAG3, MAGEA2, MAGEA2B, CSAG4, MAGEA12, CSAG1, MAGEA3, CETN2, NSDHL, ZNF185, PNMA5, PNMA3, PNMA6A, MAGEA1, PNMA6F, ZNF275, MIR12129, LOC105373378, PNMA6E, ZFP92, TREX2, HAUS7, ECMXP, BGN, ATP2B3, CCNQ, LOC105373383, DUSP9, PNCK, SLC6A8, BCAP31, ABCD1, PLXNB3, SRPK3, IDH3G, SSR4, PDZD4, L1CAM, LCA10, AVPR2, ARHGAP4, NAA10, RENBP, HCFC1, HCFC1-AS1, TMEM187, MIR3202-1, MIR3202-2, IRAK1, MIR718, MECP2, OPN1LW, OPN1MW2, OPN1MW, OPN1MW3, TEX28, TKTL1, FLNA, EMD, RPL10, SNORA70, DNASE1L1, TAZ, CH17-340M24.3, ATP6AP1, GDI1, FAM50A, MIR6858, PLXNA3, LAGE3, UBL4A, SLC10A3, FAM3A, G6PD, IKBKG, FAM223A, FAM223B, CTAG1A, CTAG1B, CTAG2, GAB3, DKC1, SNORA36A, MIR664B, SNORA56, MPP1, SMIM9, F8, H2AB1, H2AB2, H2AB3, F8A3, F8A1, F8A2, MIR1184-1, MIR1184-2, MIR1184-3, FUNDC2, CMC4, MTCP1, BRCC3, VBP1, RAB39B, CLIC2, LOC101927830, TMLHE-AS1, TMLHE, SPRY3, VAMP7, IL9R

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
- 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 [redacted]

A portion of this analysis was performed at the following location(s):
ARUP Laboratories Site [redacted]

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.

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
Maternal Contamination Study Fetal Spec	23-167-118588	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Maternal Specimen	23-167-118588	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Cytogenomic SNP Microarray - Fetal	23-167-118588	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00

END OF CHART

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