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

Physician: Doctor, Example

Patient: Patient, Example

DOB	5/3/2020
Gender:	Female
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	00/00/0000 00:00

Cytogenomic SNP Microarray

ARUP test code 2003414

Cytogenomic SNP Microarray

Abnormal * (Ref Interval: Normal)

Test Performed: Cytogenomic SNP Microarray (CMA SNP)
Specimen Type: Peripheral blood
Indication for Testing: Right aortic arch, Anomalous origin of subclavian artery

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RESULT SUMMARY
Abnormal Microarray Result (Female)

22q11.2 Deletion (DiGeorge/Velocardiofacial syndrome)

Classification: Pathogenic
Copy number change: 22q11.21 loss
Size: 2.5 Mb

RESULT DESCRIPTION
This analysis showed an interstitial deletion (1 copy present) involving chromosome 22, within 22q11.21. This region includes at least 74 genes (listed below), including the gene TBX1.

Deletion of this region is associated with the 22q11.2 deletion syndrome, also known as DiGeorge/velocardiofacial syndrome (DGS/VCFS), involving recurrent breakpoints within flanking low-copy repeat regions A and D. The reported size of this deletion may vary across studies due to variability in breakpoints within flanking repeat regions.

INTERPRETATION
This result is consistent with a clinical diagnosis of 22q11.2 deletion syndrome. Features associated with this disorder may include congenital heart defects (particularly conotruncal malformations), palatal abnormalities, characteristic facial features, developmental delay/intellectual disability, behavioral difficulties, immune deficiency due to absent or hypoplastic thymus, and hypocalcemia due to parathyroid hypoplasia (which may lead to seizures). Other findings may include feeding and swallowing problems, GI, renal, CNS, and skeletal anomalies, as well as hearing loss, growth hormone deficiency, autoimmune disorders, ophthalmologic abnormalities, enamel hypoplasia, autism, and psychiatric illness (particularly schizophrenia).

Up to 10 percent of 22q11.2 deletions are inherited, sometimes from a mildly affected or unaffected parent. Parental FISH testing is recommended to evaluate the potential origin of this deletion and for recurrence risk counseling.

Recommendations:
1) Genetic counseling

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

2) Parental testing for the deletion by FISH analysis. This test is available, at a charge, through ARUP Laboratories. Please order test code 2002299, Chromosome FISH, Metaphase and request the DiGeorge probe.

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

References and Resources:
1) McDonald-McGinn et al. 22q11.2 deletion syndrome. GeneReviews. 2013. (www.ncbi.nlm.nih.gov/books/NBK1523/). PMID: 20301696.
2) Burnside. 22q11.21 Deletion Syndromes: A review of proximal, central, and distal deletions and their associated features. Cytogenet Genome Res 2015;146(2):89-99. PMID: 26278718.
3) McDonald-McGinn and Sullivan. Chromosome 22q11.2 deletion syndrome
(DiGeorge syndrome/velocardiofacial syndrome). Medicine (Baltimore). 2011 Jan;90(1)1-18. PMID: 21200182.
4) Bassett et al. Practical guidelines for managing patients with 22q11.2 deletion syndrome. J Pediatr. 2011 Aug;159(2):332-9. PMID: 21570089.
5) Fung et al. Practical guidelines for managing adults with 22q11.2 deletion syndrome. Genet Med. 2015 Aug;17(8):599-609. PMID: 25569435.
6) The International 22q11.2 Deletion Syndrome Foundation. (www.22q.org)
7) Unique: Understanding Rare Chromosome and Gene Disorders. (www.rarechromo.org)

Cytogenetic Nomenclature (ISCN):
arr[GRCh37] 22q11.21(18916827_21465662)x1

Genes within the 22q11.21 deleted region:
PRODH, DGCR5, DGCR9, DGCR10, DGCR2, DGCR11, ESS2, TSSK2, GSC2, LINC01311, SLC25A1, CLTCL1, HIRA, MRPL40, C22orf39, UFD1, CDC45, CLDN5, LINC00895, SEPT5, SEPT5-GP1BB, GP1BB, TBX1, GNB1L, RTL10, TXNRD2, COMT, MIR4761, ARVCF, TANGO2, MIR185, DGCR8, MIR3618, MIR1306, TRMT2A, MIR6816, RANBP1, SNORA77B, ZDHHC8, CCDC188, LOC284865, LINC00896, RTN4R, MIR1286, DGCR6L, LOC101927859, FAM230A, GGTLC3, TMEM191B, PI4KAP1, RIMBP3, LINC01660, ZNF74, SCARF2, KLHL22, MED15, POM121L4P, TMEM191A, PI4KA, SERPIND1, SNAP29, CRKL, LINC01637, AIFM3, LZTR1, THAP7, THAP7-AS1, TUBA3FP, P2RX6, SLC7A4, MIR649, P2RX6P, LRRC74B, BCRP2

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)
- AOH may be present due to 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 these 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)

Data Sharing
In cooperation with the National Institutes of Healths effort to improve understanding of specific genetic variants, ARUP submits HIPAA-compliant, de-identified (cannot be traced back to the patient) genetic test results and health information to public databases. The confidentiality of each sample is maintained. If you prefer that your test result not be shared, call ARUP Laboratories at (800) 242-2787 ext. 3301. Your de-identified information will not be disclosed to public databases after your request is received, but a separate request is required for each genetic test. Additionally, patients have the opportunity to participate in patient registries and research. To learn more, visit ARUPs Genetics website at www.aruplab.com/genetics.

This result has been reviewed and approved by [redacted]

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INTERPRETIVE INFORMATION: CYTOGENOMIC SNP MICROARRAY

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

EER Cytogenomic SNP Microarray	EERUnavailable

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
Cytogenomic SNP Microarray	20-226-111812	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
EER Cytogenomic SNP Microarray	20-226-111812	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00

END OF CHART

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