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

Physician: Doctor, Example

Patient: Patient, Example

DOB	12/31/1752
Sex:	Unknown
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	01/01/2017 12:34

Cytogenomic SNP Microarray Buccal Swab

ARUP test code 2006267

Cytogenomic SNP Microarray Buccal Swab

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

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Test Performed: Cytogenomic SNP Microarray-Buccal Swab (CMA
BUCCAL)
Specimen Type: Buccal
Indication for Testing: Autistic disorder
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RESULT SUMMARY
Abnormal Microarray Result-Likely Clinically Significant (Male)

16p13.11 Deletion (BP2 to BP3 Region)

Classification: Likely Pathogenic, Low Penetrance
Copy number change: 16p13.11 loss
Size: 773 kb
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RESULT DESCRIPTION
This analysis showed an interstitial deletion (1 copy present)
involving chromosome 16, within 16p13.11. This region contains 9
genes: BMERB1, MARF1, MIR6506, MIR484, NDE1, MYH11, CEP20,
ABCC1, and ABCC6. Of these genes, 7 are protein-coding.

This is a deletion of the 16p13.11 region, involving recurrent
breakpoints (BPs) within flanking low-copy repeat regions, BP2
and BP3. Note this region is sometimes referred to as Interval
II in the literature. The reported size of this deletion may
vary across studies due to variability in breakpoints within
flanking repeat regions.

INTERPRETATION
Deletion of 16p13.11 has been reported in association with
variable clinical phenotypes. The clinical presentation ranges
from apparently unaffected to expression of a variety of
relatively nonspecific features. Features observed across
affected carriers typically include developmental
delay/intellectual disability (including speech delay),
microcephaly, and seizures. Other clinical findings are
variable, and may include midline defects, craniofacial
dysmorphism, autism, psychiatric disorders, behavioral
difficulties, short stature, obesity, and other variable
findings. The 16p13.11 deletion has been observed in both
unaffected relatives of probands and individuals in the general
population from studies of natural genomic variation. It is
significantly enriched in patients as compared to control
populations.

Deletions involving 16p13.11 show incomplete penetrance.
Expression of any phenotype associated with this deletion has
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been estimated to be 13.1 percent (7.9121.3, 95 percent confidence interval) (Rosenfeld et al., 2013). This estimate does not define the risk for a specific phenotype but includes all levels of expression that have been observed amongst carriers of the deletion. Thus, it is possible this finding is unrelated to the indication for testing.

Note that certain genes within this patients deleted interval also confer autosomal recessive disease risk. Correlation of the patient's phenotype with the clinical features of these recessive conditions may be considered. Online tools available to assist in the identification of candidate recessive genes within this deletion: www.sivotecbioinformatics.com/ and omim-search.broadinstitute.org/. If indicated, additional molecular testing may be warranted, as microarray technology cannot identify all types of pathogenic variants.

One hypothesized explanation for the reduced penetrance and variable expressivity of copy number variants (CNVs) is that expression of clinical phenotypes may require a second hit in genes that affect the same developmental pathways. Although undefined, this second hit may be another CNV, a sequence variant, or involve environmental, epigenetic, or stochastic factors. Thus, in the absence of associated clinical findings, this CNV may represent a susceptibility factor for expression of associated phenotypes.

Deletions involving 16p13.11 are usually inherited, often from an unaffected or mildly affected parent. Parental testing is unlikely to determine if this CNV is clinically significant, as its presence or absence in a clinically unaffected parent or sibling will neither rule out nor confirm causality; however, it may be considered for recurrence risk counseling.

Recommendations:
1) Genetic counseling
2) Parental testing for the deletion by genomic microarray analysis may be considered. This test is available, at a charge, through ARUP Laboratories. Please order test code 3005694, Cytogenomic SNP Microarray, Family-Specific Variant, and include the accession number for this case.

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

References:
1) Hannes et al. Recurrent reciprocal deletions and duplications of 16p13.11: the deletion is a risk factor for MR/MCA while the duplication may be a rare benign variant. J Med Genet. 2009 Apr;46(4):223-32. PMID: 18550696.
2) Heinzen et al. Rare deletions at 16p13.11 predispose to a diverse spectrum of sporadic epilepsy syndromes. Am J Hum Genet. 2010 May 14;86(5):707-18. PMID: 20398883.
3) Liu et al. Neuropathology of 16p13.11 deletion in epilepsy. PLoS One. 2012;7(4):e34813. PMID: 22523559.
4) Nagamani et al. Phenotypic manifestations of copy number variation in chromosome 16p13.11. Eur J Hum Genet. 2011 Mar;19(3):280-6. PMID: 21150890.
5) Tropeano et al. Male-biased autosomal effect of 16p13.11 copy number variation in neurodevelopmental disorders. PLoS One. 2013 Apr 18;8(4):e61365. PMID: 23637818.
6) Redaelli et al. Refining the Phenotype of Recurrent Rearrangements of Chromosome 16. Int J Mol Sci. 2019 Mar 4;20(5):1095. PMID: 30836598.
7) Ullmann et al. Array CGH identifies 16p13.11 duplications and deletions that predispose to autism and/or mental retardation. Hum Mutat 2007; 28:674-82. PMID: 17480035.
8) Kendall et al. Cognitive performance and functional outcomes of carriers of pathogenic copy number variants: analysis of the UK Biobank. Br J Psychiatry. 2019 May;214(5):297-304. PMID:

30767844.
9) de Kovel et al. Recurrent microdeletions at 15q11.2 and 16p13.11 predispose to idiopathic generalized epilepsies. Brain. 2010 Jan;133(Pt 1):23-32. PMID: 19843651.
10) Ingason et al. Copy number variations of chromosome 16p13.1 region associated with schizophrenia. Mol Psychiatry. 2011 Jan;16(1):17-25. PMID: 19786961.
11) Cooper et al. A copy number variation morbidity map of developmental delay. Nat Genet 2011; 43: 838-846.PMID: 21841781.
12) Rosenfeld et al. Estimates of penetrance for recurrent pathogenic copy-number variations. Genet Med. 2013 Jun;15(6):478-81. PMID: 23258348.
13) Unique: Understanding Rare Chromosome and Gene Disorders. (www.rarechromo.org)

Cytogenomic Nomenclature (ISCN):
arr[GRCh37] 16p13.11(15516148_16289059)x1

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 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 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 Health's 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 ARUP's Genetics website at www.aruplab.com/genetics.

This result has been reviewed and approved by

INTERPRETIVE INFORMATION: Cytogenomic SNP Microarray
Buccal Swab
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
Cytogenomic SNP Microarray Buccal Swab	25-148-105582	5/28/2025 10:15:00 AM	5/28/2025 10:53:39 AM	5/28/2025 10:56:00 AM

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

END OF CHART

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