ARUP LABORATORIES | aruplab.com
500 Chipeta Way, Salt Lake City, Utah 84108-1221
phone: 801-583-2787, toll free: 800-522-2787
Tracy I. George, MD, Chief Medical Officer

Patient Report

Patient Age/Sex: Male

Specimen Collected: 20-Dec-21 09:52

X-Cytogenomic SNP Microarray |Received: 21-Dec-21 10:33 Report/Verified: 21-Dec-21 10:42

Procedure	Result	Units	Reference Interval
Cytogenomic SNP Microarray	**Abnormal** * f1 i1		Normal

Result Footnote

f1: Cytogenomic SNP Microarray
Test Performed: Cytogenomic SNP Microarray (CMA SNP)
Specimen Type: Peripheral blood
Indication for Testing: Congenital malformation, unspecified; 46,XY,add(13)(q32.3)

RESULT SUMMARY
Abnormal Microarray Result (Male)

Terminal Deletion 13q

Classification: Pathogenic
Copy number change: 13q33.2q34 loss
Size: 8.8 Mb

RESULT DESCRIPTION
This analysis showed a terminal deletion (1 copy present) involving chromosome 13 within 13q33.2q34. This region contains at least 88 genes (listed below).

This pattern of abnormality is suggestive of a terminal deletion of chromosome 13q, consistent with the concurrent chromosome analysis reported under ARUP accession XX-XXX-XXXXXX.

INTERPRETATION
Terminal deletion of 13q is associated with a variable clinical phenotype that may include developmental delay/intellectual disability, microcephaly, craniofacial dysmorphism, hypotonia, epilepsy, skeletal anomalies, and cardiac and genitourinary/anorectal malformations. Clinical correlation should be performed with careful consideration, as the size of the deletions reported in the literature may vary from the deletion reported here.

Note that certain genes within this patient’s 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 are www.sivotecbioinformatics.com/ and omim-search.broadinstitute.org/. If indicated, additional testing (sequencing) is warranted, as microarray technology cannot identify all types of pathogenic variants.

This deletion may represent an isolated abnormality or an unbalanced rearrangement involving sequences outside of probe coverage on the array, which may be de novo or inherited. Therefore, parental FISH analysis is recommended to evaluate the potential origin of this deletion and for recurrence risk counseling.

Recommendations:
1) Genetic counseling
2) Parental testing by chromosome analysis. 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.

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

Result Footnote

f1: Cytogenomic SNP Microarray

References:
1) Sagi-Dain et al. The rare 13q33-q34 microdeletions: eight new patients and review of the literature. Hum Genet. 2019 Oct;138(10):1145-1153. PMID: 31321490.
2) He et al. Reduced anogenital distance, hematuria and left renal hypoplasia in a patient with 13q33.1-34 deletion: case report and literature review. BMC Pediatr. 2020 Jul 2;20(1):327. PMID: 32616040.
3) Wang et al. Chromosome 13q deletion syndrome involving 13q31-qter: A case report. Mol Med Rep. 2017 Jun;15(6):3658-3664. PMID: 28393221.
4) Reinstein et al. Terminal microdeletions of 13q34 chromosome region in patients with intellectual disability: Delineation of an emerging new microdeletion syndrome. Mol Genet Metab. 2016 May;118(1):60-3. PMID: 27067448.
5) Kirchhoff et al. Phenotype and 244k Array-CGH characterization of chromosome 13q deletions: an update of the phenotypic map of 13q21.1-qter. Am J Med Genet A 2009; 149A:894-905. PMID: 19363806
6) Quelin et al. Twelve new patients with 13q deletion syndrome: genotype-phenotype analyses in progress. Eur J Med Genet 2009; 52:41-6. PMID: 19022413
7) Walczak-Sztulpa et al. Chromosome deletions in 13q33-34: report of four patients and review of the literature. Am J Med Genet A. 2008 Feb 1;146A(3):337-42. PMID: 18203171.
8) UNIQUE disorder leaflet on deletions including the end of 13q (available at https://www.rarechromo.org/media/information/Chromosome%2013/13q%20deletions%20including%20the%20end%20of%2013q%20FTNW.pdf).

Cytogenomic Nomenclature (ISCN):
arr[GRCh37] 13q33.2q34(106321647_115107733)x1

Genes within the 13q33.2q34 deleted region:
LINC00343, LINC00460, EFNB2, ARGLU1, LINC00551, LINC00443, FAM155A, SNORD31B, MIR1267, FAM155A-IT1, LIG4, ABHD13, TNFSF13B, MYO16, MYO16-AS1, LINC00399, LINC00676, IRS2, LINC00396, LOC105370361, COL4A1, COL4A2, MIR8073, COL4A2-AS2, COL4A2-AS1, RAB20, NAXD, CARS2, ING1, LINC00567, LOC105370362, PRECSIT, ANKRD10, LINC00431, LINC00368, ARHGEF7-AS2, ARHGEF7, ARHGEF7-AS1, LOC101060553, TEX29, LINC02337, LINC00354, SOX1-OT, SOX1, LOC100506016, LINC01070, LOC101928730, LINC01043, LINC01044, SPACA7, TUBGCP3, ATP11AUN, ATP11A, ATP11A-AS1, MCF2L-AS1, MCF2L, F7, F10, F10-AS1, PROZ, PCID2, CUL4A, MIR8075, LAMP1, GRTP1, GRTP1-AS1, LOC101928841, ADPRHL1, DCUN1D2, TMCO3, TFDP1, ATP4B, GRK1, LINC00552, TMEM255B, GAS6-AS1, GAS6, GAS6-DT, LINC00454, LINC00452, LINC00565, RASA3, CDC16, MIR548AR, MIR4502, UPF3A, CHAMP1, LINC01054

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)

Result Footnote

f1: Cytogenomic SNP Microarray

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 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 Bo Hong, MD, FACMG

Test Information

i1: Cytogenomic SNP Microarray
INTERPRETIVE INFORMATION: CYTOGENOMIC SNP MICROARRAY

*=Abnormal, #=Corrected, C=Critical, f=Result Footnote, H-High, i-Test Information, L-Low, t-Interpretive Text, @=Performing lab

Test Information

i1: Cytogenomic SNP Microarray

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.

*=Abnormal, #=Corrected, C=Critical, f=Result Footnote, H-High, i-Test Information, L-Low, t-Interpretive Text, @=Performing lab