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

Physician: Doctor, Example

Patient: Patient, Example

DOB	11/28/1940
Sex:	Male
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	01/01/2017 12:34

Chromosome Analysis, Leukemic Blood with Reflex to Genomic Microarray

ARUP test code 2007131

Chromosome Analysis, Leukemic Blood

See Note (Ref Interval: Normal)

Test Performed: Chromosome Analysis
Specimen Type: Peripheral Blood
Indication for Testing: CLL

Number of cells counted: N/A
Number of cells analyzed: N/A
Number of cells karyotyped: N/A
ISCN band level: N/A
Banding method: G-Banding

No metaphase cells

This specimen is being reflexed to genomic microarray

Diagnostic Impression:
Attempts in the analysis of culture preparations of bone peripheral blood failed to yield metaphase cells.

This result has been reviewed and approved by [redacted]

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

INTERPRETIVE INFORMATION: Chromosome Analysis, Leukemic Blood
Test developed and characteristics determined by ARUP Laboratories. See Compliance Statement B: aruplab.com/CS

EER Chrom Analysis LKB w/Rflx to Array

See Note

Access ARUP Enhanced Report using the link below:

-Direct access:

Cytogenomic SNP Microarray - Oncology

ARUP test code 2006325

Cytogenomic Microarray SNP - Oncology

Abnormal * (Ref Interval: Normal)

Test Performed: Cytogenomic SNP Microarray - Oncology (CMA ONC)

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

Specimen Type: Peripheral blood
Indication for Testing: CLL

RESULT SUMMARY
Abnormal Microarray Result (Male)

Clinically Significant CNVs and/or ROH (Tier 1 and Tier 2 Variants):

- Mosaic Copy-Neutral Loss of Heterozygosity (CN-LOH) 11q13.1q25

RESULT DESCRIPTION
This analysis showed a terminal region of homozygosity involving chromosome 11q13.1q25 (70.2 Mb, 780 genes, including ATM and KMT2A (MLL)).

This abnormality was observed at 40-50 percent in the sample, consistent with a somatic (acquired) origin and copy neutral loss-of-heterozygosity (CN-LOH).

INTERPRETATION
CN-LOH involving 11q has been reported in both lymphoid and myeloid malignancies, including CLL, MDS, and AML. The proposed mechanisms for CN-LOH in carcinogenesis include unmasking mutations of tumor suppressor genes, as well as providing a selective advantage to cells harboring gain-of-function mutations in some proto-oncogenes.

Please correlate this result with clinical and other laboratory findings.

Recommendation:
If warranted, monitor for LOH by genomic microarray in future studies.

References:
1) Chun et al. Assessing copy number aberrations and copy-neutral loss-of-heterozygosity across the genome as best practice: An evidence-based review from the Cancer Genomics Consortium (CGC) working group for chronic lymphocytic leukemia. Cancer Genet. 2018 Dec;228-229:236-250. PMID: 30554732.
2) O'Keefe et al. Copy neutral loss of heterozygosity: a novel chromosomal lesion in myeloid malignancies. Blood. 2010 Apr 8;115(14):2731-9. PMID: 20107230.
3) Makishima H and Maciejewski JP. Pathogenesis and consequences of uniparental disomy in cancer. Clin Cancer Res. 2011 Jun 15;17(12):3913-23. PMID: 21518781.

Cytogenetic Nomenclature (ISCN):
arr[GRCh37] 11q13.1q25(64732849_134942626)x2 mos hmz

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 a loss- or absence-of-heterozygosity (LOH or AOH)
- Copy-neutral LOH (CN-LOH) may be present due to acquired UPD (segmental or whole chromosome)
- AOH may be present due to parental relatedness (consanguinity) or uniparental disomy (UPD)
- The detection sensitivity (resolution) for any particular genomic region may vary dependent upon tumor burden, 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
- Genome-wide resolution varies from approximately 25-50 kb for copy number changes and approximately 3 Mb for ROH for samples with high tumor content (generally greater than 70 percent), to several Mb for samples with lower tumor content (20-30 percent)
- The limit of detection for clonality (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
- Variant analysis is performed in accordance with recommendations by the American College of Medical Genetics and Genomics (ACMG), using tiered classification terminology
- Acquired/somatic or constitutional/germline cancer-associated copy number variants (CNVs) and ROH are classified and reported using the following clinical significance categories: Clinically Significant CNVs and/or ROH (Tier 1 and Tier 2 Variants) and Other Clonal Variants (Tier 3)
- Constitutional/germline CNVs not associated with cancer are classified according to the ACMG recommended 5-tier classification system: pathogenic, likely pathogenic, variant of uncertain significance (VUS), likely benign, and benign
-In general, only constitutional CNVs classified as pathogenic or likely pathogenic will be reported using the following clinical significance category: Other Variants (Likely Constitutional)
- Constitutional CNVs conferring non-cancer recessive disease risk will generally not be reported
- CNVs classified as Tier 4, likely benign or benign that are devoid of relevant gene content or reported as common findings in the general population, are generally not reported
- ROH are generally reported when known or suspected to be mosaic and representative of CN-LOH
- Total autosomal homozygosity (only autosomal ROH greater than 3 Mb are considered for this estimate) consistent with AOH at a level of greater than 10 percent will generally be reported; AOH less than 10 percent may be reported, dependent upon on the concern for masked CN-LOH and/or a recessive disorder

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)

This result has been reviewed and approved by [redacted]

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

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

INTERPRETIVE INFORMATION: Cytogenomic Microarray
SNP - Oncology
Test developed and characteristics determined by ARUP Laboratories. See Compliance Statement B: aruplab.com/CS

EER CMA ONC — EERUnavailable

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
Chromosome Analysis, Leukemic Blood	20-344-157212	12/9/2020 1:53:00 PM	12/11/2020 12:55:23 PM	12/18/2020 3 25:00 PM
EER Chrom Analysis LKB w/Rflx to Array	20-344-157212	12/9/2020 1:53:00 PM	12/11/2020 12:55:23 PM	12/18/2020 3 25:00 PM
Cytogenomic Microarray SNP - Oncology	20-344-157212	12/9/2020 1:53:00 PM	12/18/2020 3:24:38 PM	12/31/2020 10:39:00 AM
EER CMA ONC	20-344-157212	12/9/2020 1:53:00 PM	12/18/2020 3:24:38 PM	12/31/2020 10:39:00 AM

END OF CHART

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