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

Physician: Doctor, Example

Patient: Patient, Example

DOB	8/5/1932
Gender:	Male
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	00/00/0000 00:00

Cytogenomic SNP Microarray - Oncology

ARUP test code 2006325

Cytogenomic Microarray SNP - Oncology

Abnormal * (Ref Interval: Normal)

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Test Performed: Cytogenomic SNP Microarray - Oncology (CMA ONC)
Specimen Type: Bone marrow
Indication for Testing: B-ALL
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RESULT SUMMARY
Abnormal Microarray Result (Male)

Clinically Significant CNVs and/or ROH (Tier 1 and Tier 2
Variants):
- Interstitial Deletions (Losses) within 7p12.2 (involving
IKZF1), 9p21.3p13.2 (including CDKN2A/B, PAX5 and likely
resulting in PAX5::MLLT3 fusion), and 20q11.21q13.32
- Multiple Noncontiguous Interstitial Losses within 5q
(including NR3C1)

Other Clonal Variants (Tier 3):
- Interstitial Deletions (Losses) within 2q32.1q32.2,
13q22.3q31.1, and 13q31.1
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RESULT DESCRIPTION
The above abnormalities were observed at approximately 60-80
percent in the sample, consistent with a somatic (acquired)
origin.

INTERPRETATION
This is a complex genomic profile with multiple recurrent
findings observed in B-cell acute lymphoblastic leukemia
(B-ALL), including deletions of IKZF1, CDKN2A/B, and NR3C1. The
9p deletion identified in this study has one breakpoint within
PAX5 and the other breakpoint adjacent to MLLT3, which may
result in either a partial deletion of PAX5 or a possible
PAX5::MLLT3 fusion.

Deletion of IKZF1 is typically associated with a poor prognosis
in B-ALL.

Please correlate these results with clinical and other
laboratory findings.

Recommendation:
Monitor for these abnormalities by genomic microarray analysis
in future studies.

References:
1) Mullighan et al. Deletion of IKZF1 and prognosis in acute
lymphoblastic leukemia. N Engl J Med. 2009 Jan 29;360(5):470-80.
PMID: 19129520.
2) Stanulla et al. IKZF1plusDefines a New Minimal Residual
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H=High, L=Low, *=Abnormal, C=Critical

Disease-Dependent Very-Poor Prognostic Profile in Pediatric B-Cell Precursor Acute Lymphoblastic Leukemia. J Clin Oncol. 2018 Apr 20;36(12):1240-1249. PMID: 29498923.
3) Jia Z et al. PAX5alterations in B-cell acute lymphoblastic leukemia. Front Oncol. 2022 Oct 25;12:1023606. PMID: 36387144.
4) Fazio G et al. Three novel fusion transcripts of the paired box 5 gene in B-cell precursor acute lymphoblastic leukemia. Haematologica. 2015 Jan;100(1):e14-7. PMID: 25304615.
5) Ghazavi et al. Molecular basis and clinical significance of genetic aberrations in B-cell precursor acute lymphoblastic leukemia. Exp Hematol. 2015 Aug;43(8):640-53. PMID: 26101161.
6) Fedullo et al. Prognostic implications of additional genomic lesions in adult Philadelphia chromosome-positive acute lymphoblastic leukemia. Haematologica. 2019 Feb;104(2):312-8. PMID: 30190342.
7) Hollings et al. Deletion 20q in association with Philadelphia chromosome positive acute lymphoblastic leukemia. A report of two cases. Cancer Genet Cytogenet. 1995 Jan;79(1):32-5. PMID: 7850748.

Cytogenomic Nomenclature (ISCN):
arr[GRCh37] 2q32.1q32.2(188480307_190363144)x1-2
arr[GRCh37] 5q21.2q22.1(103068468_110365350)x1-2
arr[GRCh37] 5q31.3q32(140206744_145688332)x1-2
arr[GRCh37] 5q32(146600210_148951064)x1-2
arr[GRCh37] 5q34(167807673_167835465)x1-2
arr[GRCh37] 5q34q35.1(167864762_172220393)x1-2
arr[GRCh37] 5q35.1(172342986_172405033)x1-2
arr[GRCh37] 7p12.2(50411762_50468721)x1-2
arr[GRCh37] 9p21.3p13.2(20626498_36928914)x1-2
arr[GRCh37] 13q22.3q31.1(77702333_80687591)x1-2
arr[GRCh37] 13q31.1(80904553_80923801)x1-2
arr[GRCh37] 20q11.21q13.32(30647051_57113459)x1-2

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]

INTERPRETIVE INFORMATION: Cytogenomic Microarray
SNP - Oncology

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.

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
Cytogenomic Microarray SNP - Oncology	23-232-103082	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00

END OF CHART

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