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PATIENT REPORT

Patient Age/Sex: Male

Specimen Collected: 5/2/2025 15:24 MDT

Cytogenomic MIP Array FFPE Oncology	**Received: 5/6/2025 09:25 MDT**		**Report/Verified: 5/6/2025 09:26 MDT**
Procedure	**Result**	**Units**	**Reference Interval**
Block ID	A1		

Cytogenomic MIP Array FFPE Oncology	**Received: 5/6/2025 09:25 MDT**		**Report/Verified: 5/6/2025 09:52 MDT**
Procedure	**Result**	**Units**	**Reference Interval**
Cytogenomic MIP Array,FFPE	**Abnormal** * f1 i1		[Normal]

Result Footnote

f1: Cytogenomic MIP Array, FFPE
Test Performed: Cytogenomic Molecular Inversion Probe Array, FFPE Tissue – Oncology (FFPEARRAY)
Specimen Type: Tumor Kidney
Estimated Tumor Content: 80 percent
Indication for Testing: Wilms Tumor

RESULT SUMMARY
Abnormal Microarray Result (Male)

Clinically Significant CNVs and/or ROH (Tier 1 and Tier 2 Variants):
- CN-LOH 11p (including 11p15.5 imprinting locus WT1 at 11p13

**Negative for CNVs/LOH 1p, 1q, 16q, and 17p

RESULT DESCRIPTION
This analysis showed a terminal region of homozygosity within 11p (20.6 Mb, 396 genes, including the imprinting locus associated with Beckwith-Wiedemann syndrome and the gene WT1), consistent with copy-neutral loss of heterozygosity (CN-LOH).

This abnormality was observed at a high percentage in this sample. Therefore, it is uncertain whether it represents an acquired or constitutional origin.

NOTE: Due to the provided indication, chromosomes 1p, 1q, 16q, and 17p were scrutinized during this analysis.

INTERPRETATION
These findings are recurrent in Wilms tumor (WT). CN-LOH 11p may represent an unfavorable biomarker in WT depending on risk stratification. Additionally, due to the percentage observed, this specific finding may be acquired or constitutional. Constitutional CN-LOH 11p is associated with Beckwith-Wiedemann syndrome (BWS), a growth disorder with variable presentation and risk for WT and other embryonal tumors in childhood. Clinical correlation and additional follow-up testing may be warranted.

Recommendation:
Clinical correlation and consideration for 11p15 methylation testing to evaluate for BWS, if warranted. This test is available, at a charge, through ARUP Laboratories. Please order test code 3001635, Beckwith-Wiedemann Syndrome (BWS) and Russell-Silver Syndrome (RSS) by Methylation-Specific MLPA.

References:
1) NCCN Guidelines Version 1.2023. Wilms Tumor (Nephroblastoma).
2) Pater et al. Wilms tumor. Pediatr Blood Cancer. 2021 May;68 Suppl 2:e28257. PMID: 32893998.
3) Dome et al. Risk stratification for Wilms Tumor: current approach and future directions. Am Soc Clin Oncol Educ Book. 2014:215-23. PMID: 24857079.
4) Dome et al. Advances in Wilms Tumor Treatment and Biology: Progress Through International

Result Footnote

f1: Cytogenomic MIP Array, FFPE

Collaboration. J Clin Oncol. 2015 Sep 20;33(27):2999-3007. PMID: 26304882.
5) Perlman et al. WT1 mutation and 11P15 loss of heterozygosity predict relapse in very low-risk wilms tumors treated with surgery alone: a children's oncology group study. J Clin Oncol. 2011 Feb 20;29(6):698-703. PMID: 21189373.

Cytogenetic Nomenclature (ISCN):
arr[GRCh37] 11p15.5p15.1(192764_20765467)x2 hmz

Technical Information
- This assay was performed using the OncoScan(TM) CNV Assay (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)
- 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 OncoScan CNV array contains over 220,000 SNP probes with a median probe density (kb/probe) of 16-19 kb
- Genome-wide resolution varies from approximately 300-400 kb for copy number changes and approximately 5 Mb for ROH for samples with high tumor content to several Mb for samples with lower tumor content (greater than 50 percent tumor content is recommended for this assay)
- 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 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 5 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.

Result Footnote

f1: Cytogenomic MIP Array, FFPE

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 30 percent)
- Balanced chromosomal rearrangements (translocations, inversions and insertions)
- Genomic imbalance in repetitive DNA regions (centromeres, telomeres, segmental duplications, and acrocentric chromosome short arms)

Test Information

i1: Cytogenomic MIP Array, FFPE

INTERPRETIVE INFORMATION: Cytogenomic Molecular Inversion Probe Array, FFPE Tissue - Oncology

For detection of copy number alterations and loss of heterozygosity in FFPE specimens.

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.