SNP Array

SAMPLE REPORT

Ambry Genetics
A TEMPUS COMPANY

PATIENT
Legal Name: **Patient, Sample**
Accession #: 00-091024
DOB: 01/01/2017
Sex Assigned at Birth: Male
MRN: N/A
Indication: Diagnostic

TEST INFORMATION
Portal Order #: 000000
Family #: 000000
Specimen #: N/A
Specimen type: Blood EDTA
Collection date: 00/00/2025
Received date: 00/00/2025
Test Started: 00/00/2025
Final Report: 00/00/2025

MEDICAL PROFESSIONAL
Physician, Sample, MD
Sample Facility

ADDITIONAL RECIPIENTS
Client, Sample

POSITIVE: Pathogenic CNV Detected

Results

Change	Chromosome Region	Classification	Genomic Coordinates	Min Size	Max Size
GAIN	**17p11.2**	**Pathogenic**	**16761827 - 20304681**	**3.543 Mb**	**3.548 Mb**

SNP Array Result: arr[GRCh37] 17p11.2(16761827_20304681)x3

Interpretation

COPY NUMBER VARIATIONS

Variant description:

The results of this test indicate an interstitial copy number **GAIN** (see min/max size above) at **17p11.2** that involves 81 gene(s) (see RefSeq genes below), including *RAI1*.

Region summary:

This copy gain overlaps the **Potocki-Lupski syndrome** region. Potocki-Lupski syndrome is characterized by global developmental delay, speech impairment, intellectual disability, infantile hypotonia, oral-pharyngeal dysphasia, failure to thrive in infancy or early childhood, gastroesophageal reflux disease (GERD), autistic features, hypermetropia, cardiovascular anomalies, and sleep apnea. When parental testing was available, the variant was frequently determined to be *de novo*; however, some copy gains have been noted to be inherited (Potocki, 2007; Treadwell-Deering, 2010; Zhang, 2010; Potocki, 2017).

Based on the available evidence, this variant is classified as pathogenic.

Genetic testing for pathogenic variants in family members can be helpful in identifying at-risk individuals.

REGIONS OF HOMOZYGOSITY

No significant regions of homozygosity were detected.

Genetic counseling is a recommended option for all patients undergoing genetic testing.

Electronically Signed By Sample Director, on 00/00/0025 at 0:00:00 PM

All content hereafter is supplemental information to the preceding report.

References

- Potocki L, *et al.* (2007) *Am J Hum Genet* **80**(4):633-49. **PMID:**17357070
- Potocki L, *et al.* *GeneReviews* 2017 Aug 24 . **PMID:**28837307
- Treadwell-Deering DE, *et al.* (2010) *J Dev Behav Pediatr* **31**(2):137-43. **PMID:**20110824
- Zhang F, *et al.* (2010) *Am J Hum Genet* **86**(3):462-70. **PMID:**20188345

RefSeq Genes

Genes marked below with an asterisk (*) represent internally characterized genes determined to be associated with an autosomal recessive condition(s). However, unless specifically addressed in the interpretation section of this report, the impact of the CNV(s) regarding carrier status has not been evaluated and can be pursued if deemed clinically necessary.

The **17p11.2** region contains 81 gene(s): *TBC1D27*, *TNFRSF13B**, *LOC284191*, *LINC02090*, *MPRIP*, *PLD6*, *FLCN*, *COPS3*, *NT5M*, *MED9*, *RASD1*, *PEMT*, *SMCR2*, *RAI1*, *RAI1-AS1*, *SMCR5*, *SREBF1*, *MIR6777*, *MIR33B*, *TOM1L2*, *DRC3*, *ATPAF2*, *GID4*, *DRG2*, *LOC105371566*, *MYO15A**, *ALKBH5*, *LLGL1*, *FLII*, *MIEF2*, *TOP3A**, *SMCR8*, *SHMT1*, *MIR6778*, *EVPLL*, *LINC02076*, *KRT17P5*, *KRT17P2*, *KRT16P1*, *LGALS9C*, *USP32P2*, *FAM106A*, *CCDC144B*, *TBC1D28*, *ZNF286B*, *FOXO3B*, *TRIM16L*, *FBXW10*, *TVP23B*, *LOC101929141*, *PRPSAP2*, *SLC5A10*, *FAM83G*, *GRAP*, *SNORD3B-1*, *SNORD3B-2*, *LOC102724624*, *SNORD3D*, *GRAPL*, *LOC79999*, *SNORD3A*, *SNORD3C*, *LOC388436*, *EPN2*, *EPN2-IT1*, *EPN2-AS1*, *B9D1**, *MIR1180*, *MAPK7*, *MFAP4*, *RNF112*, *SLC47A1*, *SNORA59B*, *SLC47A1P2*, *ALDH3A2**, *SLC47A2*, *ALDH3A1*, *ULK2*, *AKAP10*, *SPECC1*, *CCDC144CP*.

SNP Array Assay Information

General Information: Genomic imbalances are an underlying cause of congenital anomalies, developmental delay, intellectual disability, autism, dysmorphism and numerous genetic syndromes. Routine karyotype analysis can detect some common chromosomal imbalances such as aneuploidies but cannot detect smaller DNA rearrangements. Chromosomal Microarray Analysis (CMA) is a technique that allows for high resolution genome-wide detection of unbalanced structural and numerical chromosomal abnormalities. In addition, SNP probes are used to detect copy-neutral chromosomal changes, such as regions of homozygosity (ROH), including patterns consistent with uniparental disomy (UPD), consanguinity, and/or identity by descent. Importantly, not all copy-neutral chromosomal changes will be detectable by the methodology due to the underlying genetic mechanism. The level of resolution of SNP Array depends primarily on the number and spacing of the oligonucleotide probes on the array.

Methodology: Genomic deoxyribonucleic acid (gDNA) is isolated from the patient’s specimen using a standardized kit, quantified, labeled and hybridized to an oligonucleotide array with more than 1.9 million copy number probes and nearly 750,000 SNP probes used for genotyping and copy number analysis. This array allows for detection of loss of copy number (deletion), gain of copy number (duplication), and regions of homozygosity.

Analytical Range: The Ambry CMA: SNP Microarray (Affymetrix® CytoScan™ HD Array, Santa Clara, CA) backbone probe spacing is set at an average of 1.1 kb throughout the entire human genome with an average of 880 basepairs in intragenic regions. This array can detect copy losses greater than 25 kb spanning at least 25 consecutive probes and copy gains greater than 50 kb spanning at least 50 consecutive probes. Copy losses of size greater than 200 kb and copy gains of size greater than 400 kb are reported, unless the copy number variant (CNV) is classified as benign or likely benign based on a multifactorial classification scheme or if the region does not include any coding sequence. CNVs that do not contain known or suspected disease-associated genes or regions are not routinely reported. Smaller, non-mosaic copy number changes may be reported when it includes a gene(s) with potential clinical relevance. The array detects currently known microdeletion/duplication syndromes, UPD due to isodisomy, and most disorders detected by chromosomal analysis and FISH tests, excluding balanced rearrangements and polyploidy. Genomic regions with low complexity or significant sequence homology may have decreased probe density and/or analytic sensitivity. Copy number variants restricted to the pseudoautosomal regions of the sex chromosomes are not routinely reported. Copy number neutral ROHs greater than 10 Mb in size and interstitial or greater than 5 Mb and telomeric are reported on the autosomes. ROH totaling 2.5% or greater of the covered autosomes will be reported.

Expected (Normal) Value: Diagnostic: No significant copy number changes or regions of homozygosity were detected. Family History or Carrier Screen: No significant copy number changes or regions of homozygosity were detected.

Result Reports: The CNV location is reported by region and location on the chromosome, and includes the min/max size (Mb) of the span of loss or gain. Minimum size (Min size Mb/kb) represents the distance between the first deviated proximal and last deviated distal probes of the CNV. Maximum size (Max size Mb/kb) represents the distance between the first non-deviated proximal and distal probes flanking the CNV, and genomic coordinates are reported based on the combination of the deviated copy number and SNP probes at the CNV boundaries. Array nomenclature is based on the ISCN (International System for Human Cytogenetic Nomenclature) 2024 guidelines. Analysis is based on genome assembly GRCh 37/hg19. CNVs in the following classifications are always reported and are based on the following definitions:

- **Pathogenic:** CNV with sufficient evidence to classify as pathogenic.
- **Likely Pathogenic:** CNV with strong evidence in favor of pathogenicity.
- **Uncertain Clinical Significance:** CNV with limited and/or conflicting evidence regarding pathogenicity.

Gender identity (if provided) is not used in the interpretation of results, and sex assigned at birth is used in the interpretation of results only when necessary.

Reclassification Reports: The SNP array analysis and CNV(s) classification and interpretation are performed based on the information and literature available as of the date the proband SNP array report was issued. Over time, as new information evolves and becomes available, the CNV(s) classification and interpretation may change. Clients should recontact the laboratory with any pertinent changes in clinical phenotype and periodically to determine if a reported variant has been reclassified. An unsolicited reclassification report may also be issued if the laboratory identifies new information that impacts the overall classification and interpretation of the reported SNP array results.

Resources:
The following references are used in copy number variation classification when applicable for observed variants.

1. HGMD® [Internet]: Stenson PD et al. *Genome Med*. 2009;1(1):13 World Wide Web URL: www.hgmd.cf.ac.uk.
2. Online Mendelian Inheritance in Man, OMIM®. McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University (Baltimore, MD), Copyright® 1966-2017. World Wide Web URL: http://omim.org
3. DECIPHER: Database of Chromosomal Imbalance and Phenotype in Humans using Ensembl Resources. Firth, H.V. *et al.*, 2009. Am.J.Hum.Genet 84, 524-533 (DOI: dx.doi.org/10/1016/j.ajhg.2009.03.010)
4. Database of Genomic Variants: MacDonald JR, et al. *Nucleic Acids Res* 2014 Jan;42(Database issue):D986-92. World Wide Web URL: http://dgv.tcag.ca/dgv/app/home
5. UCSC Genome Browser: Kent WJ, et al. *Genome Res* 2002 Jun;12(6):996-1006. World Wide Web URL: https://genome.ucsc.edu/
6. ClinGen. Rehm H.L, et al. *N Engl J Med* 2015 372(23):2235-42. World Wide Web URL: https://www.clinicalgenome.org/

Disclaimer: This test was developed, and its performance characteristics were determined by Ambry Genetics Corporation. It has not been cleared or approved by the US Food and Drug Administration. The FDA does not require this test to go through premarket FDA review. It should not be regarded as investigational or for research. This test should be interpreted in context with other clinical findings. The Ambry Test: SNP Array will only detect net gain or loss of genomic material and regions of homozygosity (ROH) meeting reporting criteria and therefore is not intended to analyze the following types of chromosomal aberrations: balanced translocations, Robertsonian translocations, balanced insertions, inversions, point mutations, low level mosaicism, epigenetic abnormalities, heterodisomic or mosaic UPD or any microdeletions and duplications that are under the resolution of the array or not represented on the array. Breakpoints may be platform-specific and impacted by technical or analytical variations. A negative result from the analysis cannot rule out the possibility that a tested individual carries an aberration in the undetectable group. Although molecular tests are highly accurate, rare diagnostic errors may occur. Possible diagnostic errors include sample mix-up, technical errors, and clerical errors. This report does not represent medical advice. Any questions, suggestions, or concerns regarding interpretation of results should be forwarded to a genetic counselor, medical geneticist, or physician skilled in interpretation of the relevant medical literature. This laboratory is certified under the Clinical Laboratory Improvement Amendments (CLIA) as qualified to perform high complexity clinical laboratory testing.