ARUP LABORATORIES | www.aruplab.com
500 Chipeta Way, Salt Lake City, Utah 84108-1221
phone: (801) 583-2787, toll free: (800) 522-2787
Julio C. Delgado, MD, MS, Director of Laboratories

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

Physician: Doctor, Example

Patient: Patient, Example

DOB	5/11/1989
Gender:	Female
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	00/00/0000 00:00

Childhood-Onset Epilepsy Panel, Sequencing and Deletion/Duplication

ARUP test code 2007545

Ordering Physician Name	TEST, TEST Performed by: GeneDx 207 Perry Parkway Gaithersburg, MD 20877 Anne Maddalena, Ph.D.,FACMG,
Ordering Physician Phone Number	8002422787 Performed by: GeneDx 207 Perry Parkway Gaithersburg, MD 20877 Anne Maddalena, Ph.D.,FACMG,
Childhood-Onset Epilepsy Panel	NEGATIVE Date Test(s) Started: 12/11/2018 17:19:00 Test(s) Requested: Childhood Epilepsy Panel / Sequencing and Deletion/Duplication Analysis Result: NEGATIVE: No Pathogenic Variant was Detected. No pathogenic variant known to be associated with childhood-onset epilepsy was identified in this patient by sequencing and deletion/duplication analysis of the genes in this panel. See the attached table for a list of genes included in the panel. Interpretation: Pathogenic variants in the genes included in this panel cause Mendelian forms of epilepsy with onset in childhood. Many of these genes encode subunits of ion channels involved in stabilizing or propagating neuronal activity, including components of the voltage-gated sodium and calcium channels and the ligand-gated gamma-aminobutyric (GABA) and nicotinic acetylcholine receptor channels (ref. 1-4). The panel also includes non-ion channel genes, many of which are involved in transcriptional activation or repression and cause neurotransmitter disorders, neurometabolic disorders, and syndromic forms of epilepsy (ref. 1, 3-7). The clinical sensitivity of sequencing and deletion/duplication analysis of the genes included in the Childhood Epilepsy Panel depends on the patient's clinical phenotype. Overall, 17-20% of epileptic encephalopathies have an identifiable genetic etiology (ref. 8). Specific information about the diagnostic yield for each gene in selected populations is summarized in the attached table. This negative result does not rule out a genetic basis for epilepsy in this patient. It is possible that this

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

individual has a pathogenic variant in a portion of a gene that is not included in the analysis or in a gene that is not included in this panel.
Recommendation: If not already performed, whole genome oligonucleotide array CGH analysis could be considered, as genomic imbalances have been identified in up to 8% of patients with epileptic encephalopathy and 9% of patients with idiopathic generalized and focal epilepsies (ref 9-11). If clinically indicated, exome sequencing could be considered and is reported to be positive in 37-39% of individuals with epilepsy (ref 12-13). Genetic counseling is recommended.
Resources: GenomeConnect is an NIH initiative created to enable individuals and families with the same genetic variant or medical history to connect and share de-identified information. If you are interested in participating, please visit www.genomeconnect.org.
Methods: Genomic DNA from the submitted specimen was enriched for the complete coding regions and splice site junctions of the genes on this panel using a proprietary targeted capture system developed by GeneDx for next generation sequencing with CNV calling (NGS-CNV). The enriched targets were simultaneously sequenced with paired-end reads on an Illumina platform. Bi-directional sequence reads were assembled and aligned to reference sequences based on NCBI RefSeq transcripts and human genome build GRCh37/UCSC hg19. After gene specific filtering, data were analyzed to identify sequence variants and most deletions and duplications involving coding exons For the CHRNA7 and MAGI2 gene(s), deletion/duplication analysis, but not sequencing was performed since only large deletions have been reported in these genes. For the FOXG1 and SLC6A8 gene(s), sequencing but not deletion/duplication analysis, was performed. Alternative sequencing or copy number detection methods were used to analyze regions with inadequate sequence or copy number data by Next generation sequencing (NGS). Reported clinically significant variants were confirmed by an appropriate method. Sequence and copy number variants are reported according to the Human Genome Variation Society (HGVS) or International System for Human Cytogenetic Nomenclature (ISCN) guidelines, respectively. Reportable variants include pathogenic variants, likely pathogenic variants and variants of uncertain significance. Likely benign and benign variants, if present, are not routinely reported but are available upon request.
Report electronically signed by: Dianalee McKnight PhD, FACMG
References: 1. Nicita et al., (2011) Seizure: Eur J Epilepsy doi: 10.1016/j.seizure.2011.08.007; 2. Deprez et al. (2009) Neurology 72: 273-281; 3. Macdonald et al. (2010) J Physiol 588: 1861-1869; 4. Andrade DM. (2009) Hum Genet 126: 173-193; 5. Ottman et al. (2010) Epilepsia 51: 655-670; 6. Ramachandran et al. (2009) Epilepsia 50: 29-36; 7. Steinlein et al. (2004) Nat Rev Neurosci 5: 401-408; 8. EpiPM Consortium (2015) Lancet Neurol 14: 1219-28; 9. Mefford et al. (2011) Annals Of Neurology 70 (6): 974-85 (PMID: 22190369); 10. Mefford et al. (2010) PLoS Genetics 6 (5): e1000962 (PMID: 20502679); 11. Olson et al. (2014) Ann. Neurol. 75 (6): 943-58 (PMID: 24811917); 12. Helbig et al. (2016) Genet. Med. 18 (9): 898-905; 13. Lee et al. (2014) JAMA 312 (18): 1880-7
Limitations: Genetic testing using the methods applied at GeneDx is expected to be highly accurate. Normal findings do not rule out the diagnosis of a genetic disorder since some genetic abnormalities may be undetectable by this test. The methods used cannot reliably detect deletions of 20bp to 500bp in size, or insertions of 10bp to 500 bp in size. Sequencing cannot detect low-level mosaicism. The copy number assessment methods used with this test cannot reliably detect mosaicism and cannot identify balanced chromosome aberrations. Rarely, incidental findings of large chromosomal rearrangements outside the gene of interest may be identified. Regions of certain genes have inherent sequence properties (for example: repeat, homology, or pseudogene regions, high GC content, rare polymorphisms) that yield suboptimal data, potentially impairing accuracy of the results. False negative results may also occur in the setting of bone marrow transplantation, recent blood transfusion, or

suboptimal DNA quality. As the ability to detect genetic variants and naming conventions can differ among laboratories, rare false negative results may occur when no positive control is provided for testing of a specific variant identified at another laboratory. The chance of a false positive or false negative result due to laboratory errors incurred during any phase of testing cannot be completely excluded. Interpretations are made with the assumption that any clinical information provided, including family relationships, are accurate. Consultation with a genetics professional is recommended for interpretation of results.
Disclaimer: This test was performed at GeneDx, 207 Perry Parkway, Gaithersburg, MD 20877. Laboratory data interpretation was performed at either GeneDx or BioReference Laboratories, 481 Edward H. Ross Drive, Elmwood Park, NJ 07407.
Performed by: GeneDx
207 Perry Parkway
Gaithersburg, MD 20877

Anne Maddalena, Ph.D.,FACMG,

EER Childhood-Onset Epilepsy Panel

See Note

Access ARUP Enhanced Report using either link below:

-Direct access:

-Enter Username, Password: https://erpt.aruplab.com
Username:
Password:

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
Ordering Physician Name	18-345-105215	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Ordering Physician Phone Number	18-345-105215	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Childhood-Onset Epilepsy Panel	18-345-105215	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
EER Childhood-Onset Epilepsy Panel	18-345-105215	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00

END OF CHART

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