

## Epilepsy and Seizure Disorders Panel: Sequencing and CNV Analysis

**Test Code:** MEPI1

**Turnaround time:** 6 weeks

**CPT Codes:** 81404 x1, 81406 x1, 81405 x1, 81175 x1, 81302 x1, 81403 x1, 81407 x1, 81409 x1, 81479 x1

### Condition Description

Epilepsy is defined as a disorder in which an individual has recurrent, unprovoked seizures. It has a prevalence of about 5-10 per 1000 people. While the causes of epilepsy are diverse, a significant proportion are considered to be genetic in origin. Epilepsy can occur as part of a clinical spectrum that is associated with a particular genetic syndrome, such as Mowat Wilson syndrome, Dravet syndrome, and "chromosomal" epilepsies. Common "chromosomal" epilepsies include 1p36 deletion syndrome, Wolf-Hirschhorn syndrome, Angelman syndrome, Miller-Dieker syndrome, 15q inversion-duplication, Down syndrome and ring chromosome 14 and 20. In addition, epilepsy can occur as an isolated finding, 40% of which are believed to be due to genetic causes. Approximately 2% of the genetic causes of isolated epilepsy are due to monogenetic causes while the rest are thought to be due to multifactorial genetic and environmental causes. Of the monogenetic genes identified, the majority code for ion channel subunits and neurotransmitter receptors.

The Epilepsy and Seizure Disorders Panel is comprised of a next generation sequencing (NGS) for syndromic and non-syndromic causes of seizures. It is recommended that individuals with seizures have a chromosomal microarray as a first tier test. Please click here for information on our [EmArray Cyto](#) and [CytoScan SNP Array](#).

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### References:

- Michelucci *et al.*, (2012), *Curr Neurol Neurosci Rep*, 12:445-455.
- Nicita *et al.*, (2012), *Seizure*, 21:3-11.
- Pal *et al.*, (2010), *Nat Rev Neurol*, 6:445-453.
- Pandolfo, (2011), *Semin Neurol*, 31:506-518.
- Poduri and Lowenstein, (2011), *Curr Opin Genet Dev*, 21:325-332.

### Genes

[ABAT](#), [ADGRG1](#), [ADSL](#), [AKT3](#), [ALDH5A1](#), [ALDH7A1](#), [ALG13](#), [ANKRD11](#), [ARHGFE9](#), [ARX](#), [ASPM](#), [ASXL1](#), [ATP1A2](#), [ATP1A3](#), [ATP6AP2](#), [BCKDK](#), [CACNA1A](#), [CACNA1E](#), [CACNA2D2](#), [CACNB4](#), [CASK](#), [CASR](#), [CDKL5](#), [CENPJ](#), [CHD2](#), [CHRNA2](#), [CHRNA4](#), [CHRN2B](#), [CLCN4](#), [CLN3](#), [CLN5](#), [CLN6](#), [CLN8](#), [CNTNAP2](#), [CPA6](#), [CSTB](#), [CTSD](#), [CYP27A1](#), [DCX](#), [DEPDC5](#), [DNAJC5](#), [DNM1](#), [DNM1L](#), [DYRK1A](#), [EEF1A2](#), [EFHC1](#), [EHMT1](#), [EPM2A](#), [FLNA](#), [FOLR1](#), [FOXG1](#), [GABRA1](#), [GABRB1](#), [GABRB2](#), [GABRB3](#), [GABRG2](#), [GAMT](#), [GATM](#), [GNAO1](#), [GOSR2](#), [GRIN1](#), [GRIN2A](#), [GRIN2B](#), [HCN1](#), [HCN4](#), [HNRNPU](#), [IQSEC2](#), [KANS1](#), [KCNA1](#), [KCNA2](#), [KCNB1](#), [KCNC1](#), [KCNH1](#), [KCNJ10](#), [KCNJ11](#), [KCNMA1](#), [KCNQ2](#), [KCNQ3](#), [KCNT1](#), [KCTD7](#), [LGI1](#), [LIAS](#), [MAGI2](#), [MBD5](#), [MECP2](#), [MEF2C](#), [MFSD8](#), [MTHFR](#), [MTOR](#), [NDE1](#), [NDUFA1](#), [NEDD4L](#), [NEXMIF](#), [NHLRC1](#), [NPRL2](#), [NPRL3](#), [NRXN1](#), [OPHN1](#), [PACS1](#), [PAFAH1B1](#), [PCDH19](#), [PHF6](#), [PIGA](#), [PIK3CA](#), [PLCB1](#), [PNKP](#), [PNPO](#), [POLG](#), [PPT1](#), [PRICKLE1](#), [PRICKLE2](#), [PRRT2](#), [PURA](#), [QARS1](#), [RELN](#), [SCARB2](#), [SCN1A](#), [SCN1B](#), [SCN2A](#), [SCN3A](#), [SCN8A](#), [SCN9A](#), [SHH](#), [SIK1](#), [SIX3](#), [SLC13A5](#), [SLC19A3](#), [SLC25A19](#), [SLC25A22](#), [SLC2A1](#), [SLC35A2](#), [SLC6A1](#), [SLC9A6](#), [SMARCA2](#), [SMC1A](#), [SNAP25](#), [SPTAN1](#), [ST3GAL3](#), [ST3GAL5](#), [STIL](#), [STX1B](#), [STXBP1](#), [SYN1](#), [SYNGAP1](#), [SZT2](#), [TBC1D24](#), [TCF4](#), [TPP1](#), [TSC1](#), [TSC2](#), [TSEN54](#), [UBE3A](#), [USP9X](#), [WDR45](#), [WDR62](#), [WVVOX](#), [ZEB2](#)

### Indications

This test is indicated for:

- Individuals with epilepsy.

### Methodology

**Next Generation Sequencing:** In-solution hybridization of all coding exons is performed on the patient's genomic DNA. Although some deep intronic regions may also be analyzed, this assay is not meant to interrogate most promoter regions, deep intronic regions, or other regulatory elements, and does not detect single or multi-exon deletions or duplications. Direct sequencing of the captured regions is performed using next generation sequencing. The patient's gene sequences are then compared to a standard reference sequence. Potentially causative variants and areas of low coverage are Sanger-sequenced. Sequence variations are classified as pathogenic, likely pathogenic, benign, likely benign, or variants of unknown significance. Variants of unknown significance may require further studies of the patient and/or family members.

**Copy Number Analysis:** Comparative analysis of the NGS read depth (coverage) of the targeted regions of genes on this panel was performed to detect copy number variants (CNV). The accuracy of the detected variants is highly dependent on the size of the event, the sequence context and the coverage obtained for the targeted region. Due to these variables and limitations a minimum validated CNV size cannot be determined; however, single exon deletions and duplications are expected to be below the detection limit of this analysis.

### Detection

**Next Generation Sequencing:** Clinical Sensitivity: Unknown. Mutations in the promoter region, some mutations in the introns and other regulatory element mutations cannot be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's clinical/biochemical phenotype.

Analytical sensitivity for sequence variant detection is ~99%.

**Copy Number Analysis:** The sensitivity and specificity of this method for CNV detection is highly dependent on the size of the event, sequence context and depth of coverage for the region involved. The assay is highly sensitive for CNVs of 500 base pairs or larger and those containing at least 3 exons. Smaller (< 500 base pairs) CNVs and those that involving only 1 or 2 exons may or may not be detected depending on the sequence context, size of exon(s) involved and depth of coverage.

## Specimen Requirements

**Submit only 1 of the following specimen types**

### Type: DNA, Isolated

**Specimen Requirements:**

Microtainer

8µg

Isolation using the Perkin Elmer™ Chemagen™ Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

**Specimen Collection and Shipping:**

Refrigerate until time of shipment in 100 ng/µL in TE buffer. Ship sample at room temperature with overnight delivery.

### Type: Saliva

**Specimen Requirements:**

Oragene™ Saliva Collection Kit

Oragene™ Saliva Collection Kit used according to manufacturer instructions. Please contact EGL for a Saliva Collection Kit for patients that cannot provide a blood sample.

**Specimen Collection and Shipping:**

Please do not refrigerate or freeze saliva sample. Please store and ship at room temperature.

### Type: Whole Blood (EDTA)

**Specimen Requirements:**

EDTA (Purple Top)

Infants and Young Children ( 2 years of age to 10 years old: 3-5 ml

Older Children & Adults: 5-10 ml

Autopsy: 2-3 ml unclotted cord or cardiac blood

**Specimen Collection and Shipping:**

Ship sample at room temperature for receipt at EGL within 72 hours of collection. Do not freeze.

## Related Tests

- CytoScan + SNP and EmArray Cyto.
- Custom diagnostic mutation analysis (KM) is available to family members if mutations are identified by targeted mutation testing or sequencing analysis.
- Prenatal testing is available only for known familial mutations to individuals who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.
- Epilepsy and Seizure Disorders: Deletion/Duplication Panel.