Epilepsy and Seizure Disorders: Sequencing Panel

Test Code: MEPI1  
Turnaround time: 6 weeks  
CPT Codes: 81404 x1, 81405 x1, 81406 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. 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.

Support for the development of this panel was provided, in part, by a grant from the Epilepsy Foundation to Dr. Andrew Escayg, Associate Professor, Department of Human Genetics.

References:


Genes

- ABAT, ADGRG1, ADGRV1, ADS1, ALDH5A1, ALDH7A1, ARHGEF9, ARX, ACPM, ATP1A2, ATP6AP2, BCSDK1, CACNA1A, CACNB4, CASK, CASR, CDKL5, CENPJ, CHRNA2, CHRNA4, CHRNA5, CLN3, CLN5, CLN6, CLN8, CNTNAP2, CPAP, CSTR, CTD, CV2P27A1, DCX, DNAJC5, EFHC1, EMX2, EPM2A, FLNA, FOLR1, FOXG1, GABRA1, GABRG2, GAMT, GATM, GOSR2, GRIN2A, HCN1, HCN4, KCN1A, KCN1J1, KCNMA1, KCNQ2, KCNQ3, KCNT1, KCNT2, LGI1, LIAS, MAGI2, MBDS, MCHP1, MECP2, MEF2C, MFSDB, MTHFR, NDE1, NDUFA1, HLR1C1, NRXN1, OPHN1, PAFAH1B1, PCDH19, PHF6, PLCB1, PNKP, PNPO, POLG, PPT1, PRICKLE1, PRICKLE2, PRT2, RELN, SCARB2, SCN1A, SCN1B, SCN2A, SCN3A, SCN8A, SCN9A, SHH, SIX3, SLC19A3, SLC25A19, SLC25A22, SLC2A1, SLC9A6, SPTAN1, SPTMX2, ST3GAL3, ST3GAL5, STIL, STXBP1, SYN1, TBC1D4, TCF4, TDP1, TSC1, TSC2, TSEN55, UBE3A, WDR62, 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.

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. Large deletions/duplications will not be detected by this analysis. Results of molecular analysis
should be interpreted in the context of the patient's clinical/biochemical phenotype.

Analytical Sensitivity: ~99%.

### Specimen Requirements

Submit only 1 of the following specimen types

#### Type: Whole Blood

Specimen Requirements:

In EDTA (purple top) tube:
- Infants (2 years): 3-5 ml
- Older Children & Adults: 5-10 ml.

Specimen Collection and Shipping: Ship sample at room temperature with overnight delivery.

#### Type: Isolated DNA

Specimen Requirements:

In microtainer: 60 ug

Isolation using the Qiagen™ Puregene kit for DNA extraction is recommended.

Specimen Collection and Shipping: Refrigerate until time of shipment in 100 ng/µl of TE buffer. Ship sample at room temperature with overnight delivery.

### 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.