Neurology Panel: Sequencing and CNV Analysis

**Test Code:** MM280  
**Turnaround time:** 6 weeks  
**CPT Codes:** 81405 x1, 81406 x1, 81407 x1

**Condition Description**
Disorders that affect the nervous system include a large group of conditions with genetic and phenotypic heterogeneity. As a group, neurological disorders often have overlapping clinical features, such as intellectual disability, seizures, microcephaly, and motor disability. Other characteristics may include brain malformations (lissencephaly, molar tooth sign), vision loss, speech difficulties, and respiratory failure. This wide phenotypic spectrum can make diagnosis challenging, but obtaining a specific diagnosis is important for prognosis, patient management, and development of therapeutic strategies.

Note: This test does not detect the retrotransposon insertion in the 3’ UTR of the FKTN gene common in some Asian populations. For patients with suspected Fukuyama congenital muscular dystrophy, testing for the FKTN insertion is recommended. Analysis for the FKTN insertion is available as a separate assay.

**References:**

**Genes**
ACTG1, ADGRG1, ADSL, AH1, ALDH5A1, ALDH7A1, ARFGEP2, ARHGEF9, ARX, ASPM, ATP1A2, ATP6AP2, ATR, ATRX, BCKD, CACNB4, CASK, CC2D2A, CDC6, CDSRAP2, CDKL5, CDT1, CENPJ, CEP135, CEP162, CEP290, CEP41, CHMP1A, CHRNA2, CHRNA4, CHPN2, CLN3, CLN6, CLN8, CNTNAP2, CPA6, CSTB, CTS, CYP27A1, DCX, DHCRT7, DNAJC5, EFCB1, EHM1, EOMES, EPM2A, EXOSC3, FGF3, FGF8, FKRP, FKTN, FLNA, FOLR1, FOXG1, FOXH1, GABRA1, GABRG2, GAST, GM1T, GLI2, GSRP1, GRN2A, KCNJ10, KCMN1, KCNQ3, KCNQ2, KCNQ2, KCNQ5, KCTD7, KIF7, KIF8B, KN1L, IAML3, LARGF1, LGH1, LGI1, MAGIL, MAPK10, MBDS, MCF4, MEF2C, MFSD8, MKS1, MYCN, NDE1, NHLRC1, NIN, NODAL, NPH1, NPH1, OPHN1, ORC4, ORC6, PAFAH1B1, PCHD19, PCTN, PCLB1, PNKP, PNPO, POLG, POMMNTI, PMTM2, PPT2, PKR1, PRICKLE1, PRRT2, RB1B, RB3GAP1, RABGAP2, RARS2, RBBP8, RELN, RPPGRP1, RTTN, SCARB2, SCNI, SCN1B, SCN2A, SCN8A, SCN9A, SHH, SIX3, SLC19A3, SLC25A21, SLC25A22, SLC2A1, SLC9A6, SPTAN1, SRPX2, ST3GAL3, ST3GAL5, STL1, STXBP1, SYN1, TBC1D44, TCF4, TGIN1, TMEG138, TMEG139, TMEG176, TMEG237, TMEG67, TTP1, TSC1, TSC2, TSEN2, TSEN34, TSEN54, TUBA1A, TUBB, TUBB2B, TUBB3, VCP, VLDLR, VRK1, WDR62, ZEB2, ZIC2, ZNF335

**Indications**
This test is indicated for:
- Confirmation of a clinical diagnosis of neurological disorders.

**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 regions may also be analyzed, this assay is not meant to interrogate most promoter regions, deep intronic regions, or other regulatory elements, and other regulatory element mutations cannot be detected by this analysis. 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 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.

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. Pathogenic variants in the promoter region, some pathogenic variants in the introns and other regulatory elements 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 variant detection is ~99%.

Copy Number Sensitivity: 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 and larger and those containing at least 3 exons. Smaller (< 500 base pairs) CNVs and those 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: 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.

Type: DNA, Isolated

Specimen Requirements:
Microtainer
8µg
Isolation using the Perkin Elmer™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.

Related Tests

- Brain Malformations Panel
- Seizure Disorders Panel
- Neurology: Deletion/Duplication Panel