In-solution hybridization of all coding exons is performed on the patient's genomic DNA. Although some deep intronic insertion is recommended. Analysis for the molecular analysis should be interpreted in the context of the patient's clinical/biochemical phenotype. 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**

ACTB, ACTG1, ADGRG1, ADSS, AHI1, ALDH5A1, ALDH7A1, ARFGGEF2, ARHGEF8, ARX, ASPM, ATP1A2, ATP6AP2, ATR, ATRX, BCKDK, CACNB4, CASK, CC2D2A, CDC6, CDK5RAP2, CDKL5, CTD1, CEP99, CEP135, CEP152, CEP290, CEP41, CEP63, CHMP1A, CHRNA2, CHRNA4, CHRNA3, CLN3, CLN5, CLN6, CLN8, CNTPAP2, CPA8, CSTB, CTSD, CYP27A1, DCX, DHCR7, DISP1, DNAJC5, EFHC1, EMT1, EOMES, EPM2A, EXOSC3, ESRP, FKBP1, FKTN, FLNA, FOLR1, FOXG1, FOXH1, GABRA1, GABRG3, GAMT, GATM, GLI2, GOSR2, GRIN2A, GRIN2B, KCNJ10, KCNMA1, KCNO2, KCNQ3, KCNT1, KCTD7, KIF1BP, KIF7, KN1, LAMC3, LARGE1, LGI1, LIAS, MAGI2, MAPK10, MBD5, MCPH1, MECPR2, MEF2C, MFSD8, MKS1, MYCN, NDE1, NHLRC1, NIN, NODAL, NPHP1, NRXN1, OPHN1, ORC4, ORC6, PARAFH1B1, PCDH19, PCNT, PLG1, PNKP, PNPO, POC1A, POLG, POMGNT1, POMT1, POMT2, PPT1, PQQP1, PRICKLE1, PRRT2, PTCH1, RAB18, RAB3GAP1, RAB3GAP2, RARS2, RBBP8, RELN, RPRPPL1, RTTN, SCARB2, SCN1A, SCN1B, SCN2A, SCN8A, SCN9A, SHH, SIX3, SLC19A3, SLC25A19, SLC25A22, SLC2A1, SLC9A6, SPTAN1, SPRP2, ST3GAL3, ST3GAL5, STIL, STXBP1, SYN1, TBC1D24, TCF4, TGF1, TMEM138, TMEM216, TMEM237, TMEM87, TPP1, TSC1, TSC2, TSEN2, TSEN54, TSEN58, TUBA1A, TUBA8, TUBB2B, TUBB3, UBE3A, VCP, VDLR, VRK1, WDR62, ZEB2, ZIC2, ZNF336

**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 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. Pathogenic variants in the promoter region, some pathogenic variants 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: 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
Orangene™ 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 unclootted cord or cardiac blood

Specimen Collection and Shipping:
Ship sample at room temperature for receipt at EGL within 24 hours of collection. Do not refrigerate or freeze.

**Related Tests**
- Brain Malformations Panel
- Seizure Disorders Panel
- Neurology: Deletion/Duplication Panel