Unexplained refractory and/or suspect familial epilepsy:
All patients should have completed
- Magnetic resonance imaging (MRI)
- Electroencephalogram
Consider: metabolic or autoimmune testing based on clinical presentation (see metabolic and autoimmune testing tables)

**Family history of epilepsy with known variant**

**Order: FMTT / Familial Mutation, Targeted Testing**

- **Does the identified epilepsy include:**
  - Congenital anomalies
  - Developmental delay
  - Intellectual disability
  - Autism

**Order: CMACB / Chromosomal Microarray, Congenital, Blood**

- **Is a mitochondrial epilepsy suspected?**
  - Definitive cause found
  - Inconclusive
  - Negative

- **Order EPPAN / Comprehensive Epilepsy With or Without Encephalopathy Gene Panel, Varies**
  - Order as appropriate:
    - CSTB / CSTB Gene, Repeat Expansion Analysis, Varies
    - HMP / Hemiplegic Migraine With or Without Epilepsy Gene Panel, Varies
    - TSCP / Tuberous Sclerosis Gene Panel, Varies
    - CGPH / Custom Gene Panel, Hereditary, Next-Generation Sequencing, Varies

- **Is a myopathy present?**
  - Definitive cause found
  - Inconclusive
  - Negative

**Order on muscle biopsy:**
- Mitochondrial Full Genome Analysis by Next-Generation Sequencing (NGS)

**Consider:**
- CMITO / Combined Mitochondrial Full Genome and Nuclear Gene Panel

- **Consider WESDX / Whole Exome Sequencing for Hereditary Disorders, Varies or whole genome sequencing**

- **Mitochondrial epilepsy syndrome suspected**
  - A positive GDF15 / Growth Differentiation Factor 15 (GDF15), Plasma or FAPM / Fatty Acid Profile, Mitochondrial (C8-C18), Serum result increases the likelihood of a mitochondrial disorder

- **Specific epilepsy syndrome suspected?**

**Definitive cause found**

**Disorder-specific management**

**Perform any metabolic confirmatory assays recommended in interpretation and consider family studies for segregation analyses**

**Definitive cause found**

**Consider WESDX / Whole Exome Sequencing for Hereditary Disorders, Varies or whole genome sequencing**

**Metabolic Tests to Consider**
- AACSF / Amino Acids, Quantitative, Spinal Fluid
- AAQP / Amino Acids, Quantitative, Plasma
- CDG / Carbohydrate Deficient Transferrin for Congenital Disorders of Glycosylation, Serum
- CRDPU / Creatine Disorders Panel, Urine
- LACS1 / Lactate, Plasma
- OAU / Organic Acids Screen, Urine
- OLIDU / Oligosaccharide Screen, Urine
- PIPA / Pipecolic Acid, Serum
- PIPU / Pipecolic Acid, Urine, if newborn
- PLSD / Lysosomal and Peroxisomal Storage Disorders Screen, Blood Spot, if <18 years of age
- PXP / Fatty Acid Profile, Peroxisomal (C22-C26), Plasma
- PUPYP / Porphyrins and Pyrimidines Panel, Plasma
- PYR / Pyruvate, Blood
- PYRC / Pyruvic Acid, Blood
- PUPYP / Porphyrins and Pyrimidines Panel, Spinal Fluid

**Autoimmune Evaluations to Consider**
- EPC2 / Epilepsy, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid
- EPS2 / Epilepsy, Autoimmune/Paraneoplastic Evaluation, Serum

*CGPH / Custom Gene Panel, Hereditary, Next-Generation Sequencing, Varies can be used to modify any epilepsy panel or test any single gene included on any epilepsy panel.

**Segregation studies can be performed to determine if a variant segregates with the condition in a family and/or occurred de novo, which may clarify the significance of a variant. For more information, contact the Laboratory Genetic Counselors at 800-533-1710.