SCN1A-related Disorders: SCN1A Gene Sequencing

Test Code: SSCN1
Turnaround time: 6 weeks
CPT Codes: 81407 x1

Condition Description

SCN1A-Related Seizure Disorders
SCN1A-related seizure disorders are a spectrum that range from simple febrile seizures at the mild end to Dravet syndrome and intractable childhood epilepsy with generalized tonic-clonic seizures that are severe at the other end. A clinical diagnosis of SCN1A-related seizures disorders is difficult because the phenotypes range on a spectrum, even within the same family and many other conditions have epilepsy as a feature. Therefore, a diagnosis relies on molecular testing of the SCN1A gene (2q24). Sequencing of the SCN1A gene detects 73%-92% of mutations. Deletion/duplication analysis of the SCN1A gene detects 8-27% of mutations. Mutations are inherited in an autosomal dominant manner. Phenotypes that are commonly associated with SCN1A-related seizure disorders include febrile seizures (FS), generalized epilepsy with febrile seizures plus (GEFS+), Dravet syndrome, severe myoclonic epilepsy, borderline (SMEB), intractable childhood epilepsy with generalized tonic-clonic seizures (ICE-GTC), and infantile partial seizures with variable foci. Clinical features associated with SCN1A-related seizure disorders include one or more family members with epilepsy, especially if the epilepsy is of more than one type, febrile seizures, a history of seizures after vaccination, hemiconvulsive seizures, and seizures triggered by environmental factors. SCN1A-related seizure disorders show incomplete penetrance and variable expressivity.

Familial Hemiplegic Migraine
Familial Hemiplegic Migraine (FHM) is in the category of migraine with aura. Clinical diagnostic criteria of FHM include migraine with aura, some degree of hemiparesis, and at least one first-degree relative has identical attacks. Three genes are known to be associated with FHM: CACNA1A (FHM1), ATP1A2 (FHM2), and SCN1A (FHM3). Please note that this test is only for the SCN1A gene.

References:
- GeneReviews
- OMIM #182389: SCN1A gene
- OMIM #609634: Familial Hemiplegic Migraine
- OMIM #607208: Dravet syndrome
- OMIM #604403 and #604233: GEFS+

Genes
SCN1A

Indications
This test is indicated for:
- Confirmation of a clinical diagnosis of SCN1A-related disorders.
- Carrier testing in adults with a family history of SCN1A-related 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
Sequencing of the SCN1A gene detects 73%-92% of mutations for SCN1A-related seizure disorders. Deletion/duplication analysis of the SCN1A gene detects 8-27% of mutations for SCN1A-related seizure disorders.

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 uncultted cord or cardiac blood

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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**
- Deletion/duplication analysis of the SCN1A gene by CGH array is available for those individuals in whom sequence analysis is negative.
- 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.
- X-Linked Intellectual Disability panels are available for 30, 60, and 90+ genes.