SCN1A-related Disorders: SCN1A Gene Deletion/Duplication

**Test Code:** DSCN1  
**Turnaround time:** 2 weeks  
**CPT Codes:** 81228 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 at the severe 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 in an individual in whom sequence analysis was negative.  
- Carrier testing in adults with a family history of SCN1A-related disorders in whom sequence analysis was negative.

### Methodology

DNA isolated from peripheral blood is hybridized to a CGH array to detect deletions and duplications. The targeted CGH array has overlapping probes which cover the entire genomic region.

Please note that a "backbone" of probes across the entire genome are included on the array for analytical and quality control purposes. Rarely, off-target copy number variants causative of disease may be identified that may or may not be related to the patient's phenotype. Only known pathogenic off-target copy number variants will be reported. Off-target copy number variants of unknown clinical significance will not be reported.

### 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

* Preferred specimen type: Whole Blood

**Type: Whole Blood**

Specimen Requirements:

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

Specimen Collection and Shipping: Refrigerate until time of shipment. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Type: Saliva**

Specimen Requirements:

Oragene™ Saliva Collection kit (available through EGL) used according to manufacturer instructions.

Specimen Collection and Shipping: Store sample at room temperature. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Special Instructions**

Sequence analysis is required before deletion/duplication analysis by targeted CGH array. If sequencing is performed outside of Emory Genetics Laboratory, please submit a copy of the sequencing report with the test requisition.

**Related Tests**

- Sequence analysis of the SCN1A gene is available and is required before deletion/duplication analysis.
- 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.