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 that are 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) tube:
- Infants (2 years): 3-5 ml
- Older Children & Adults: 5-10 ml

Disclaimer: This information is confidential and subject to change without notice. It may not be reproduced in whole or part unless authorized in writing by an authorized EGL representative.
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 EGL Genetics, 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.