PCDH19-related X-linked Female-Limited Epilepsy with Mental Retardation: PCDH19 Gene Deletion/Duplication

**Test Code:** DPC19  
**Turnaround time:** 2 weeks  
**CPT Codes:** 81228 x1

**Condition Description**

Mutations in the PCDH19 gene (Xq22) (OMIM#: 300460) have been associated with epileptic encephalopathy, early infantile, 9 (OMIM#: 300088). In the original report, 15 related female patients had a grand mal convulsive disorder associated with intellectual disability. The reported age of onset varied from 4 to 18 months of age. Early symptoms included partial and generalized convulsions that were associated with developmental regression. The frequency of seizures was reported to decline at age of 2 but cognitive impairment was prominent in the affected females.

Other features reported in this family and other unrelated affected families include variable intellectual disability, neuropsychiatric disorders including autism and schizophrenia, purposeless hand movements, poor language development, and ataxia. Some obligate carrier males have been reported to display obsessive traits and interests.

One study identified PCDH19 mutations in 11 of 45 (24.4%) unrelated females with epileptic encephalopathy of infancy who were negative for mutations in the SCN1A Gene. Another study found PCDH19 mutations in 2 of 86 (2.3%) females with epilepsy with or without intellectual disability. A third study identified PCDH19 mutations in 13 of 117 (11%) females with febrile seizures and epilepsy.

For patients with suspected X-Linked Epilepsy with MR, sequence analysis is recommended as the first step in mutation identification. For patients in whom mutations are not identified by full gene sequencing, deletion/duplication analysis is appropriate.

**References:**
- OMIM# 300460: PCDH19 gene
- OMIM# 300088: X-Linked Epilepsy with MR

**Genes**

PCDH19

**Indications**

This test is indicated for:
- Confirmation of a clinical diagnosis of X-Linked Epilepsy with MR in an individual in whom sequence analysis was negative.
- Carrier testing in adults with a family history of X-Linked Epilepsy with MR 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**

Detection is limited to duplications and deletions. The CGH array will not detect point or intronic mutations. Results of molecular analysis must be interpreted in the context of the patient's clinical and/or biochemical phenotype.

**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.

**Related Tests**

- Sequence analysis of the *PCDH19* 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.