**XLMR with Cerebellar Hypoplasia and Distinctive Facial Appearance: OPHN1 Gene Deletion/Duplication**

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

### Condition Description

Mutations in the OPHN1 gene (Xq12) are associated with X-linked mental retardation with subtle facial dysmorphism and cerebellar anomalies, including hypoplasia of the vermis, expansion of the cisterna magna, and retrocerebellar cysts. Phenotypic features can include neonatal hypotonia with motor delay but no obvious ataxia, marked strabismus, early-onset complex partial seizures, and moderate to severe intellectual disability. Other affected individuals with OPHN1 mutations are reported to have moderate to severe intellectual disability associated with enlargement of the lateral ventricles and cerebellar hypoplasia, seizures, ataxia, strabismus, and hypogenitalism with cryptorchidism, hypoplastic scrotum, and microphallus.

Facial features associated with OPHN1 mutations include mild facial dysmorphism with long face, prominent forehead, deep-set eyes, marked infraorbital creases, strabismus, short or upturned philtrum, and large ears. Obligate female carriers have been reported to show subtle facial changes and/or reduced cerebellar size in some cases.

In one study, four different novel mutations were identified in the OPHN1 gene: two mutations were found in a group of 17 unrelated males with mental retardation and known cerebellar anomalies (12%) and two mutations were found in a group of 196 unrelated males with X-linked intellectual disability without previous brain imaging studies (1%). Retrospective imaging studies, when possible, detected cerebellar hypoplasia in the latter patients.

Both point mutations and deletions have been reported in the OPHN1 gene.

[Click here](#) for the OMIM summary on this condition.

### Genes

**OPHN1**

### Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of XLMR with cerebellar hypoplasia and distinctive facial appearance in individuals who have tested negative for sequence analysis
- Carrier testing in adult females with a family history of XLMR with cerebellar hypoplasia and distinctive facial appearance who have tested negative for sequence analysis

### 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) 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\textsuperscript{TM} 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

Submit copies of diagnostic biochemical test results with the sample, if appropriate. Contact the laboratory if further information is needed.

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

- Sequencing analysis of the *OPHN1* gene is available (YR) and is required before deletion/duplication analysis.
- A CGH array-based test for deletion/duplication analysis of 64 different X-linked intellectual disability genes is available (OL).
- Prenatal testing is available to adult females who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.