XLID, PTCHD1-related: PTCHD1 Gene Deletion/Duplication

**Condition Description**

Intellectual disability (ID) is a nonprogressive cognitive impairment affecting 1-3% of the Western population. It is estimated that up to 50% of moderate-severe cases have genetic causes and approximately 10% are due to X-linked intellectual disability disorders (XLID). XLID can be syndromic or nonsyndromic and is observed in all ethnic groups. More than 100 XLID syndromes have been described in the literature to date. Fragile X is the most common XLID syndrome (~1 in 4000 males) while others can be quite rare with only a few patients reported in the literature. Males can have moderate to severe intellectual disability depending on the syndrome, and carrier females can also be affected, but typically have milder clinical symptoms.

Filges et al. (2011) reports a family in which two brothers have XLID. An approximate 200kb deletion containing the *PTCHD1* (Xp22.11) gene only was identified in the brothers and their clinically unaffected mother. Additional males with disruption or mutation of the *PTCHD1* gene have been identified. Affected males have moderate to severe ID. Additional features reported include hypotonia, autistic features, and transient ataxic movement; however, as none of these features are found consistently in individuals with a mutation in the *PTCHD1* gene, it is thought that expressivity is variable. The *PTCHD1* gene is expressed in the human brain with preferential expression in the temporal lobe, cortex, and cerebellum.

Please note that the *PTCHD1* gene is not currently part of our XLID 90+ gene panel.

For patients with suspected *PTCHD1*-related XLID, 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 #300828: PTCHD1 gene
- OMIM #300830: Chromosome Xp22 Deletion syndrome

**Genes**

**PTCHD1**

**Indications**

This test is indicated for:

- Confirmation of a clinical diagnosis of *PTCHD1*-related XLID in an individual in whom sequence analysis was negative.
- Carrier testing in adults with a family history of *PTCHD1*-related XLID 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.

**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 *PTCHD1* 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.