XLMR 30: PAK3 Gene Deletion/Duplication

**Test Code:** DPAK3  
**Turnaround time:** 2 weeks  
**CPT Codes:** 81228 x1

<table>
<thead>
<tr>
<th>Condition Description</th>
</tr>
</thead>
</table>
| 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.

Mutations in the PAK3 gene have been identified in five families with XLID. Three of the mutations are missense mutations (Bienvenu et al. 2000; Gedeon et al. 2003; Peippo et al. 2007), one is a nonsense mutation (Allen et al. 1998), and one is a splice-site mutation (Rejeb et al. 2008). Common features seen in affected males for these five families include microcephaly, oral motor dysfunction with persistent drooling and inarticulate speech, and behavioral and psychiatric symptoms. Female carriers are often asymptomatic; however, they could show borderline to mild intellectual disability.

**References:**  
- OMIM #300558: XLMR 30  
- OMIM #300142: PAK3 gene  

<table>
<thead>
<tr>
<th>Genes</th>
</tr>
</thead>
</table>

**Indications**

This test is indicated for:

- Confirmation of a clinical diagnosis of XLMR 30 in an individual in whom sequence analysis was negative.
- Carrier testing in adults with a family history of XLMR 30 in whom sequence analysis was negative.

<table>
<thead>
<tr>
<th>Methodology</th>
</tr>
</thead>
</table>

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.

<table>
<thead>
<tr>
<th>Detection</th>
</tr>
</thead>
</table>

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.

<table>
<thead>
<tr>
<th>Specimen Requirements</th>
</tr>
</thead>
</table>

**Submit only 1 of the following specimen types**

**Type: DNA, Isolated**

**Specimen Requirements:**  
Microtainer 3µg  
Isolation using the Perkin Elmer™Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

**Specimen Collection and Shipping:**  
Refrigerate until time of shipment in 100 ng/µL in TE buffer. Ship sample at room temperature with overnight delivery.

**Type: Whole Blood (EDTA)**

**Specimen Requirements:**  
EDTA (Purple Top)  
Infants and Young Children (2 years of age to 10 years old): 3-5 ml  
Older Children & Adults: 5-10 ml  
Autopsy: 2-3 ml unclotted cord or cardiac blood

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:
Ship sample at room temperature for receipt at EGL within 72 hours of collection. Do not freeze.

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 $PAK3$ 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.