XLMR 58: *TSPAN7* Gene Sequencing

<table>
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<th>Test Code: STSPA</th>
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<td>Turnaround time: 6 weeks</td>
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<td>CPT Codes: 81479 x1</td>
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### 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.

Zemni et al. (2000) described a female individual with mild intellectual disability and minor autistic features. She had a balanced translocation involving the X chromosome [46,X,t(X;2)(p11.2;p21.3)]. The *TSPAN7* gene, formerly known as the *TM4SF2* gene, is located at the breakpoint on the X chromosome. *TSPAN7* transcripts from this individual were barely detectable when compared with *TSPAN7* transcripts from controls. The *TSPAN7* gene is expressed in both the fetal and adult brain.

Zemni et al. identified two other mutations in the *TSPAN7* gene in two families with XLID. Both mutations were not found in 100 control chromosomes. Males and females can have mild to moderate intellectual disability.

### References:

- OMIM #300096: TSPAN7 gene

### Genes

**TSPAN7**

### Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of XLMR 58.
- Carrier testing in adults with a family history of XLMR 58.

### Methodology

PCR amplification of 7 exons contained in the *TSPAN7* gene is performed on the patient's genomic DNA. Direct sequencing of amplification products is performed in both forward and reverse directions, using automated fluorescence deoxy sequencing methods. The patient's gene sequences are then compared to a normal reference sequence. Sequence variations are classified as mutations, benign variants unrelated to disease, or variations of unknown clinical significance. Variants of unknown clinical significance may require further studies of the patient and/or family members. This assay does not interrogate the promoter region, deep intronic regions, or other regulatory elements, and does not detect large deletions.

### Detection

Clinical Sensitivity: Unknown. Mutations in the promoter region, some mutations in the introns and other regulatory element mutations cannot be detected by this analysis. Large deletions will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's clinical and/or biochemical phenotype.

Analytical Sensitivity: ~99%

### Specimen Requirements

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

**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

**Specimen Collection and Shipping:**

Ship sample at room temperature for receipt at EGL within 24 hours of collection. Do not refrigerate or freeze.
**Type: DNA, Isolated**

**Specimen Requirements:**
- Microtainer
- 8µg

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: Saliva**

**Specimen Requirements:**
- Oragene™ Saliva Collection Kit

Oragene™ Saliva Collection Kit used according to manufacturer instructions. Please contact EGL for a Saliva Collection Kit for patients that cannot provide a blood sample.

**Specimen Collection and Shipping:**
Please do not refrigerate or freeze saliva sample. Please store and ship at room temperature.

**Related Tests**
- Deletion/duplication analysis of the \textit{TSPAN7} gene by CGH array is available for those individuals in whom sequence analysis is negative.
- 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.