XLMR 14, Syndromic: **UPF3B** Gene Deletion/Duplication

**Condition Description**

In 2007, Tarpey et al. conducted a study of individuals with mental retardation (MR) from 250 families compatible with X linkage. None of these individuals had mutations in any of the XLMR-linked genes identified at the time. Three different mutations in the **UPF3B** gene (Xq25-q26) were identified in three families. One of these families had a clinical diagnosis of FG syndrome (FGS), while the other two families had clinical diagnoses of Lujan-Fryns syndrome (LFS). They then analyzed 118 affected individuals from a cohort of families with putative XLMR and found a **UPF3B** mutation in a family with nonsyndromic XLMR. Mental retardation in these families was mild to severe.

Features present in more than half of affected males in the first three families included a slender build with poor musculature, a long and thin face, high arched palate, high nasal bridge, and pectus. Half of the affected individuals had autistic features or behavioral problems. While the clinical phenotype is variable, many of these clinical features are suggestive of LFS and FGS. The affected males from the fourth family had normal physical examinations, and were hence classified as nonsyndromic XLMR.

Carrier females had normal intelligence and normal physical examinations.

For patients with suspected XLMR 14, 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:**


**Genes**

**UPF3B**

**Indications**

This test is indicated for:

- Confirmation of a clinical diagnosis of XLMR 14 in individuals who have tested negative for sequence analysis
- Carrier testing in adult females with a family history of XLMR 14 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) 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

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

- Sequence analysis of the UPF3B gene is available 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.
- Prenatal testing is available to couples who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.