**XLMR, KDM5C-related: KDM5C Gene Deletion/Duplication**

**Condition Description**

Mutations in the KDM5C gene (Xp11.22-p11.21) have been shown to cause an X-linked recessive syndromic mental retardation syndrome. Phenotypic features that have been reported include facial hypotonia, maxillary hypoplasia, strabismus, large ears with raised lobes, big hands with large fingers and proximal thumbs, prominent and separated superior incisors, scrotal tongue, and pectus excavatum. Other features of this syndrome can include slowly progressive spastic paraplegia, epileptic seizures, short stature, microcephaly, hypermetropia, and small feet, testes, and penis. Aggressive behavior and an overfriendly and anxious character have also been reported.

The phenotype associated with mutations in the KDM5C gene is variable with regard to dysmorphism and cognitive impairment. In some families, the X-linked mental retardation seems to be nonsyndromic, with no dysmorphic features. It has been estimated that the frequency of mutations in the KDM5C gene may account for 2.8% to 3.3% of families with XLMR.

Click here for the OMIM summary on this condition.

**Genes**

KDM5C

**Indications**

This test is indicated for:

- Confirmation of a clinical diagnosis of KDM5C-related syndromic XLMR in individuals who have tested negative for sequence analysis
- Carrier testing in adult females with a family history of KDM5C-related syndromic XLMR 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™ 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 *KDM5C* gene is available (YJ) 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.