**Condition Description**

Mutations in the *KDM5C* gene (Xp11.22-p11.21) have been shown to cause an X-linked recessive syndromic mental retardation. 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.

For patients with suspected *KDM5C*-related syndromic XLMR, 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.

Click [here](#) for the OMIM summary on this condition.

**Genes**

*KDM5C*

**Indications**

This test is indicated for:

- Confirmation of a clinical diagnosis of *JARID1C*-related syndromic XLMR
- Carrier testing in adult females with a family history of *JARID1C*-related syndromic XLMR

**Methodology**

**Next Generation Sequencing:** In-solution hybridization of all coding exons is performed on the patient's genomic DNA. Although some deep intronic regions may also be analyzed, this assay is not meant to interrogate most promoter regions, deep intronic regions, or other regulatory elements, and does not detect single or multi-exon deletions or duplications. Direct sequencing of the captured regions is performed using next generation sequencing. The patient's gene sequences are then compared to a standard reference sequence. Potentially causative variants and areas of low coverage are Sanger-sequenced. Sequence variations are classified as pathogenic, likely pathogenic, benign, likely benign, or variants of unknown significance. Variants of unknown significance may require further studies of the patient and/or family members.

**Detection**

Clinical Sensitivity: Unknown. It has been estimated that the frequency of mutations in the *JARID1C* gene may account for 2.8% to 3.3% of families with XLMR. 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 biochemical phenotype.

Analytical Sensitivity: 99%

**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

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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

- Deletion/duplication analysis of the *KDM5C* gene by CGH array is available for those individuals in whom sequence analysis is negative (YK).
- A CGH array-based test for deletion/duplication analysis of 109 different X-linked intellectual disability genes is available (OL).
- 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 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.