Fragile X: FMR1 Gene Deletion/Duplication

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

## Condition Description

Expansion of a CGG triplet repeat leading to DNA methylation and silencing of the FMR1 gene is the most frequent cause of Fragile X syndrome. However, other mutations within the FMR1 gene have also been identified that cause Fragile X syndrome. These include deletions, point mutations that disrupt RNA splicing, and a missense mutation. Emory Genetics Laboratory offers full gene sequencing to detect mutations other than CGG expansion as a cause of Fragile X syndrome.

Sequencing of the FMR1 gene will only be done if the patient first tests negative for expansion of the CGG tract and FMR1 DNA methylation. The FMR1 gene consists of 17 exons. These coding exons, as well as the immediate flanking regions, are PCR amplified and sequenced in both forward and reverse strands. In addition, the entire FMR1 promoter, including the four known transcription factor binding sites and the transcription initiation site, are assessed by DNA sequencing. This analysis will therefore detect coding sequence changes, splice donor and acceptor site mutations, and changes in the promoter sequence. In addition, both small and large deletions will be detected in males. Small deletions will also be detected in females, although larger deletions of the entire gene potentially could escape detection.

It is important to note that testing for expansion of the CGG tract and FMR1 DNA methylation alone does not rule out a diagnosis of Fragile X syndrome or involvement of FMR1 in the patient's phenotype. Specialized consultation is available with Dr. Stephen Warren, an authority on FMR1, on the interpretation of missense mutations.

Please click here for the GeneReviews summary on this condition.


## Genes

**FMR1**

## Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of fragile X syndrome who have tested negative by CGG repeat analysis as well as sequencing of the FMR1 gene.
- Carrier testing in adults with a family history of fragile X syndrome who have tested negative by CGG repeat analysis as well as sequencing of the FMR1 gene.

## 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**

Please submit copies of diagnostic biochemical test results along with the sample. 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 Emory Genetics Laboratory, please submit a copy of the sequencing report with the test requisition.

**Related Tests**

- For Fragile X testing, CGG repeat analysis is the recommended first tier test. Sequencing and deletion/duplication analysis are also available and should follow CGG repeat analysis.