FRAXE Syndrome: AFF2 Gene Deletion/Duplication

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

**Condition Description**

In patients who have the cytogenetic changes of Fragile X Syndrome but lack the molecular changes characteristic of that disorder (i.e., are \( FMR1 \)-mutation negative), a second site of fragility, symbolized FRAXE, has been demonstrated to be expanded. Data suggests that an etiologic relationship may exist between FRAXE and nonspecific x-linked intellectual disability. Loss of expression of the gene \( AFF2 \) has been correlated with FRAXE expansion. Sequence analysis and deletion/duplication analysis are also available to identify mutations in the \( AFF2 \) gene.

For patients with suspected FRAXE syndrome, repeat expansion testing and methylation analysis are recommended as the first step in mutation identification. For patients in whom mutations are not identified, full gene sequencing and deletion/duplication analysis are also available.

Please note that \( AFF2 \) and \( FMR2 \) are the same gene. This test is therefore a single-gene test.

**Genes**

\( AFF2, FMR2 \)

**Indications**

This test is indicated for:

- Confirmation of a clinical/biochemical diagnosis of FRAXE syndrome in an individual in whom sequencing analysis was negative.
- Carrier testing in adult females with a family history of FRAXE syndrome in whom sequencing analysis was negative.

**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 mutations 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**

Disclaimer: This information is confidential and subject to change without notice. It may not be reproduced in whole or part unless authorized in writing by an authorized EGL representative.
Please submit copies of diagnostic biochemical test results along 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 form.

**Related Tests**

- Repeat expansion testing and methylation analysis are available and are strongly recommended as the first step in mutation identification.
- **FRAXE Syndrome**: AFF2 Gene Sequencing is required before deletion/duplication analysis.
- X-Linked Intellectual Disability Panel
- Testing for Fragile X Syndrome at the FRAXA site is available by repeat expansion/methylation analysis, \textit{FMR1} sequencing, and \textit{FMR1} deletion/duplication analysis.
- Prenatal Custom Diagnostics 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.