

Fragile X-associated Tremor/Ataxia Syndrome (FXTAS): CGG Repeat Analysis

Test Code: FJ

Turnaround time: 2 weeks

CPT Codes: 81243 x1

Condition Description

Expansion of a triplet (CGG) repeat in the *FMR1* gene causes a spectrum of disorders. *FMR1*-related disorders include fragile X syndrome, fragile X-associated tremor/ataxia syndrome (FXTAS), and *FMR1*-related premature ovarian insufficiency (POI). FXTAS is characterized by later onset progressive intention tremor and gait ataxia in males with a premutation sized CGG repeat expansion. Clinical symptoms are often categorized as parkinsonism, and patients may report tremors, balance problems, difficulty walking, and problems with short-term memory. Peripheral neuropathy and weakness of lower limb muscles have been reported. White matter lesions are typically identifiable middle cerebellar peduncles and/or brain stem using MRI. Lesions in the cerebral white matter and atrophy may also be visualized. Though not well defined, penetrance is incomplete and the onset of symptoms is age-dependant. In individuals who develop FXTAS, symptoms typically present after age 50 years of age. Men with FXTAS do not have fragile X syndrome.

The *FMR1* gene is located on the X chromosome. *FMR1*-related disorders are associated with the presence of a triplet (CGG) repeat expansion in the promoter of *FMR1* leading to methylation and subsequent inactivation of the *FMR1* gene. In individuals with normal alleles, the number of CGG repeats ranges from approximately 5-44. Repeats in this range are stable when passed from parent to child. Individuals with approximately 55-200 CGG repeats are premutation carriers. Adult males in this range are at increased risk to develop FXTAS. Daughters of men with expansions in this range are obligate carriers of expansions of similar length. The number of repeats in the premutation range is unstable and may expand when passed through female meiosis. Individuals with fragile X syndrome have over 200 CGG repeats. Males with over 200 repeats are almost always affected, while females may be more mildly affected. Mosaicism, the presence of two different sized repeats or extent of methylation, for pre and full mutation alleles has been reported in some individuals with *FMR1* full CGG expansions.

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

Genes

[FMR1](#)

Indications

This test is indicated for adult males with symptoms of FXTAS.

Methodology

The DNA surrounding the CGG repeat in the *FMR1* gene is amplified by PCR and the size of the repeat is determined by capillary electrophoresis.

Detection

All cases of FXTAS syndrome caused by CGG expansion will be detected by this assay.

Reference Range

Normal: < 44 CGG repeats, Intermediate: 45-55 CGG repeats, Premutation: 55--200 repeats, Full mutation: >200 CGG repeats

Specimen Requirements

Submit only 1 of the following specimen types

Type: DNA, Isolated

Specimen Requirements:

Microtainer

20µg

Isolation using the Perkin Elmer™ Chemagen™ Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

Specimen Collection and Shipping:

Refrigerate until time of shipment in 100 ng/µL in TE buffer. Ship sample at room temperature with overnight delivery.

Type: Whole Blood (EDTA)

Specimen Requirements:

EDTA (Purple Top)

Infants and Young Children (2 years of age to 10 years old: 3-5 ml

Older Children & Adults: 5-10 ml

Autopsy: 2-3 ml unclotted cord or cardiac blood

Specimen Collection and Shipping:

Ship sample at room temperature for receipt at EGL within 72 hours of collection. Do not freeze.

Related Tests

- Testing for fragile X syndrome (MFRAX) is indicated for males and females with symptoms of fragile X.
- *FMR1*-related premature ovarian insufficiency (MFMR1) is indicated for daughters of males diagnosed with FXTAS; women experiencing ovarian dysfunction or menopause before 40 years; or for women with sons diagnosed with fragile X.