SCHOOL OF MEDICINE
INDIANA UNIVERSITY

Department of Medical and Molecular Genetics
Division of Diagnostic Genomics

Laboratory Test Directory

Fragile X, *FMR1* mutation analysis by PCR

CPT Code(s): 81243

Service Code (IU Health): 53025441

Ordering Recommendation: *FMR1* mutation analysis is recommended for individuals with developmental delay, unexplained mental retardation, autism; females indicating primary ovarian insufficiency; males with tremor/ataxia; or carrier testing of individuals with a positive family history of *FMR1*-related disorders.

Synonyms: Fragile X syndrome, FMR1 mutation analysis, CGG repeats, FXTAS, fragile X-related tremor ataxia

Methodology: Triplet repeat primed PCR and capillary electrophoresis. Reflex Southern analysis is performed as a send-out test as needed to further characterize expanded/abnormal alleles.

Performed: Mon-Fri

Reported: 6-9 days

Specimen Requirements

Patient Preparation: None required for whole blood

Collect: Lavender (EDTA) tubes

Specimen Volume: Blood: 2-6 mL whole blood

Storage/Transport: Refrigerated/Room temperature

Unacceptable Conditions: Grossly hemolyzed or clotted

Remarks:

Stability: 2 weeks refrigerated; 1 month frozen

Reference Interval: by report

Interpretive Data

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Characteristics: Fragile X (FX) syndrome is an X-linked disorder and is the most common cause of inherited mental retardation in males. Clinical features include mild to moderate mental retardation. Behavioral problems include hyperactivity, poor eye contact, hand clapping, social anxiety, etc. Female premutation carriers may develop primary ovarian insufficiency. Male premutation carriers may develop fragile X-associated tremor/ataxia syndrome (FXTAS).

Inheritance: X-Linked dominant disorder.

Cause: Fragile X syndrome is caused by an expanded trinucleotide CGG repeat in the 5' untranslated region of *FMR1* gene, which leads to hypermethylation and inhibition of gene transcription. The normal size range is up to 44 copies of the repeat. An intermediate (or gray zone) size range exists for alleles of 45-54 repeats. Premutation alleles are 55-200 repeats and full mutations are usually greater than 200 repeats.

Incidence: 1:4000 males and 1:6000 females

Penetrance: Reduced penetrance in females.

Limitations: Some expanded alleles may fail to be recognized with a level less than 3% of total DNA. Although rare, false positive or false negative results may occur. All results should be interpreted in context of clinical findings, relevant history, and other laboratory data.

References:

1. Filipovic-Sadic S et al. A Novel FMR1 PCR Method for the Routine Detection of Low Abundance Expanded Alleles and Full Mutations in Fragile X Syndrome. Clinical Chemistry 56:399–408, 2010.
2. Maddalena A et al. Technical standards and guidelines for fragile X: the first of a series of disease-specific supplements to the Standards and Guidelines for Clinical Genetics Laboratories of the American College of Medical Genetics. 2001. Accessed 4-24-12.
3. Saul RA and Tarleton JC. FMR1-Related Disorders. GeneReviews, Bookshelf ID: NBK1384. Initial Posting: June 16, 1998; Last Revision: April 26, 2012.