

Fragile X Syndrome (FMR-1) Testing

DESCRIPTION:

- Fragile X syndrome includes mental retardation, minor facial anomalies, seizures, and behavioral problems including autistic tendencies. About 1 in 4000 males, or approximately 5% of retarded males have the syndrome, which is usually less severe in females.
- This test detects the genetic abnormality known to cause >99% of Fragile X syndrome: unstable CGG trinucleotide expansion in the DNA of the 5' noncoding region of the FMR-1 gene at chromosome Xq27.3.

REASONS FOR REFERRAL:

- Confirmation of diagnosis in a patient with consistent signs and symptoms, especially males with a positive family history of mental retardation.
- Testing is often used in a "screening" fashion since physical signs are subtle, and are difficult to recognize in affected females. Pregnant women with a family history of mental retardation in males may be suitable candidates for carrier testing.

METHOD OF ANALYSIS:

- Patient DNA is amplified by PCR and CGG allele sizes determined by a high resolution laser-induced capillary fluorescence electrophoresis system.
- Southern hybridization of probe StB12.3 to an EcoRI / EagI digest of genomic DNA detects larger expansions and assesses FMR-1 methylation.
- Results are reported within 3 weeks or less of receipt of sample; expedited on request.
- Based on Guidelines from the American College of Medical Genetics (ACMG, 1994), a comprehensive genetic evaluation of patients with mental retardation of unknown cause should include routine cytogenetic analysis as well as DNA analysis for Fragile X syndrome. Chromosome abnormalities have been identified as often as or more frequently than FMR-1 mutations in mentally retarded individuals referred for Fragile X testing.

REFERENCE RANGES:

- Normal: fewer than 45 CGG repeats, most commonly 29 or 30 CGG repeats.
- Gray Zone (inconclusive): approximately 45 to 54 repeats; offspring not at risk for full mutation.
- Premutation: approximately 55 to 200 repeats. These expand with transmission, especially through females, and may result in full mutation (affected) offspring
- Full Mutation: 230 or more CGG repeats are associated with the Fragile X syndrome in males and in approximately 50% of females. Full mutations are typically hypermethylated.

SAMPLE REQUIREMENTS:

- For DNA testing, 5 to 10 milliliters of blood (minimum 1 ml) in EDTA (purple top) tubes should be sent by overnight carrier at room temperature.
- For chromosome analysis, if indicated, at additional charge: 5 to 10 milliliters of blood (minimum 2 ml) in Sodium Heparin (green top) tube sent as above.
- Prenatal testing: two (2) confluent T25 flasks of amniocytes or cultured chorionic villi.

TEST CPT CODES:

CPT 83891 DNA extraction highly purified
CPT 83892 DNA enzymatic digestion X 2
CPT 83894 DNA separation X 2
CPT 83896 DNA nucleic acid probe
CPT 83897 DNA nucleic acid transfer
CPT 83898 DNA amplification
CPT 83912 DNA interpretation and report

Discounts from list price are available for institutional billing under contractual arrangement with the laboratory. Contact Ellen Livers at 800-447-6614 ext 7523.