TEST CHANGE

Fragile X (FMR1) with Reflex to Methylation Analysis

2009033, FRAG X PCR

Specimen Requirements:	
Patient Preparation:	
Collect:	Lavender (K2EDTA), p~~P~~ink (K2EDTA), or y~~Y~~ellow (ACD s~~S~~olution A or B)~~)~~.
Specimen Preparation:	Transport 2~~5~~ mL whole blood. (Min: 1~~.5~~ mL)
Transport Temperature:	Refrigerated. Also acceptable: Ambient.
Unacceptable Conditions:	
Remarks:	
Stability:	Room Temperature~~Ambient~~: 1 week; Refrigerated: 1 month; Frozen: Unacceptable~~6 months~~
Methodology:	Polymerase Chain Reaction/Capillary Electrophoresis
Performed:	Varies~~Sun-Sat~~
Reported:	4-14 days
Note:	If a CGG repeat of 100 or greater is detected by PCR and capillary electrophoresis~~Capillary Electrophoresis~~, methylation analysis will be added. Additional charges apply.
CPT Codes:	81243; if reflexed, add 81244
New York DOH Approval Status:	This test is New York DOH approved.

Interpretive Data:

Refer to report. ~~Background Information for Fragile X (*FMR1*) with Reflex to Methylation Analysis~~
~~Characteristics of Fragile X syndrome (FXS): Affected males have moderate intellectual disability, hyperactivity, perseverative speech, social anxiety, poor eye contact, hand flapping or biting, autism spectrum disorders and connective tissue anomalies in males. Females are usually less severely affected than males. FXS is caused by *FMR1* full mutations.~~
~~Characteristics of Fragile X Tremor Ataxia Syndrome (FXTAS): Onset of progressive ataxia and intention tremor typically after the fourth decade of life. Females also have a 21 percent risk for primary ovarian insufficiency. FXTAS is caused by *FMR1* premutations.~~
~~Incidence of FXS: 1 in 4,000 Caucasian males and 1 in 8,000 Caucasian females.~~
~~Inheritance: X-linked.~~
~~Penetrance of FXS: Complete in males; 50 percent in females.~~
~~Penetrance of FXTAS: 47 percent in males and 17 percent in females >50 years of age.~~
~~Cause: Expansion of the *FMR1* gene CGG triplet repeat.~~

Full mutation: typically >200 CGG repeats (methylated).
Premutation: 55 to approx 200 CGG repeats (unmethylated).
Intermediate: 45-54 CGG repeats (unmethylated).
Normal: 5-44 CGG repeats (unmethylated).
Clinical Sensitivity: 99 percent.
Methodology: Triplet repeat-primed polymerase chain reaction (PCR) followed by size analysis using capillary electrophoresis. Methylation-specific PCR analysis is performed for CGG repeat lengths of >100 to distinguish between premutation and full mutation alleles.
Analytic Sensitivity and Specificity: 99 percent; estimated precision of sizing for intermediate and premutation alleles is within 2-3 CGG repeats.
Limitations: Diagnostic errors can occur due to rare sequence variations. Rare *FMR1* variants unrelated to trinucleotide expansion will not be detected. A specific CGG repeat size estimate is not provided for full mutation alleles. AGG trinucleotide interruptions within the *FMR1* CGG repeat tract are not assessed.

This test was developed and its performance characteristics determined by ARUP Laboratories. It has not been cleared or approved by the US Food and Drug Administration. This test was performed in a CLIA certified laboratory and is intended for clinical purposes.

Counseling and informed consent are recommended for genetic testing. Consent forms are available online.

Phenotype	Number of CGG Repeats
Unaffected	<45
Intermediate	45-54
Premutation	55-200
Affected	>200

Reference Interval:

By report