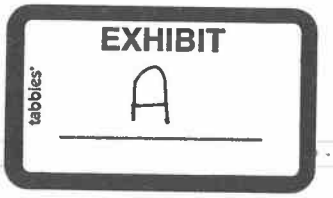

https://testdirectory.questdiagnostics.com/test/test-guides/TS_FragileX_Reflex/xsense-fragile-x-with-reflex

XSense, Fragile X with Refle...

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XSense, Fragile X with Reflex

This document summarizes information relating to this test including clinical use for diagnosis and identifying carriers and inheritance patterns, as well as methodology and test interpretation.

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(1) Related Tests

(1) Related Guides

TOP OF PAGE

Reference ranges are provided as general guidance only. To interpret test results use the reference range in the laboratory report.

The tests listed by specialty and category are a select group of tests offered. For a complete list of Quest Diagnostics tests, please adjust the filter options chosen, or refer to our Directory of Services.

Test Summary

XSense®, Fragile X with Reflex

Clinical Use

- Identify fragile X syndrome (FXS) carriers
- Determine an individual's risk of having a child with FXS
- Diagnose FXS postnatally

Clinical Background

Fragile X syndrome is the most common inherited cause of developmental delay and intellectual disability, occurring in approximately 1 in 2,500 to 3,700 males and 1 in 7,000 females.[1]

Affected males usually have moderate to severe intellectual disability, learning disabilities, attention deficit hyperactivity disorder (ADHD), depression, and difficult peer relationships.[2] In addition, boys with FXS often exhibit autism-spectrum disorders beginning in the 2nd or 3rd year of life.[3] Affected females have a variable phenotype that can range from normal intelligence to severe intellectual disability (depending upon X chromosome inactivation), with or without learning disabilities or behavioral concerns. Women who are premutation (Table 1) carriers may have fragile X-associated primary ovarian insufficiency (POI), including premature ovarian failure (POF), for which fertility evaluation and early intervention are important.[4]

In more than 99% of cases, FXS is caused by a loss-of-function variant of the *FMR1* gene located on the X chromosome.[4] Loss of function is caused by an expansion of a polymorphic CGG trinucleotide repeat in the 5' untranslated region of the *FMR1* gene, resulting in hypermethylation of the *FMR1* promoter.[5] Hypermethylation causes silencing of the *FMR1* gene and therefore correlates negatively with the level of protein expression (absent in affected males and substantially reduced in affected females), which plays a role in brain synaptic development. The severity of the phenotype is related to the extent of expansion and hypermethylation (Table 1).[4,6]

Determining the extent of hypermethylation can help determine premutation or full mutation status in rare cases in which the number of CGG repeats is near the borderline value of 200.[6] It can also detect a mosaic condition in which the CGG repeat number is in the full mutation range but subpopulations of cells have no hypermethylation (known as methylation mosaicism).[6] A person with methylation mosaicism may have less severe symptoms than a person with a hypermethylated full mutation.[6]

Other rare *FMR1* mutations associated with FXS include large deletions, point mutations, and missense mutations.

Table 1. Number of CGG Repeats in *FMR1* and Associated Phenotype

Approximate Number of CGG Repeats[a]	Hypermethylation	Classification	Gene Function	Phenotype
5 to 44	Not present	Normal	Normal	Not affected
45 to 54	Not present	Intermediate ("gray zone")	Normal	Not affected
55 to 200	Not present	Premutation	Larger premutations may have decreased gene expression	Males: ~40% incidence of FXTAS after age 50 years[2] Females:~20% incidence of POI[4]; ~21% incidence of

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CHANGE SERVICE AREA

XSense®, Fragile X with Reflex

Test Code

16313

CPT Code(s)*

81243

Physician Attestation of Informed Consent

This germline genetic test requires physician attestation that patient consent has been received if ordering medical facility is located in AK, DE, FL, GA, IA, MA, MN, NV, NJ, NY, OR, SD or VT or test is performed in MA.

Test information shown is for Service Area Quest Nichols Institute - Chantilly, VA CHANGE

Clinical Significance

Fragile X syndrome (FXS OMIM # 300624) is the most common inherited mental retardation syndrome, affecting approximately 1:4000 males and approximately 1:8000 females. The disease is caused by the expansion of a trinucleotide CGG repeat in the 5'-untranslated (UTR) region of the FMR1 gene. Methylation of the expanded CGG tract leads to silencing of expression of the FMR1 gene. The American College of Medical Genetics defines a normal repeat length as between 5 and 44. Intermediate alleles of between 45-54 repeats almost never expand to full mutations in a single meiosis. Premutation alleles are ...

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Test Resources

Test FAQ
XSense, Fragile X with Reflex

Test Summary
XSense, Fragile X with Reflex

Algorithm
Laboratory Evaluation of Developmental Delay/Intellectual Disability (DD/ID)

Includes

If Fragile X, PCR result is not Normal, or Gray zone, then Fragile X Methylation Analysis will be performed at an additional charge (CPT codes(s): 81244)

Methodology

Polymerase Chain Reaction (PCR) with Detection by Capillary Electrophoresis

Preferred Specimen(s)

4 mL whole blood collected in EDTA (lavender-top) tube

Alternative Specimen(s)

Acid citrate dextrose ACD-A-B (yellow-top), or sodium heparin (green-top) tube

Quest Diagnostics

XSense®, Fragile X with Reflex and Chromosome Analysis, Blood

Test Code

16326

CPT Code(s)*

88230**, 88262**, 81243**

**CPT Code is subject to a MEDICARE LIMITED COVERAGE POLICY and may require a signed ABN when ordering.

Physician Attestation of Informed Consent

This germline genetic test requires physician attestation that patient consent has been received if ordering medical facility is located in AK, DE, FL, GA, IA, MA, MN, NV, NJ, NY, OR, SD or VT or test is performed in MA.

Not offered in Quest Infectious Disease Inc. - San Juan Capistrano, CA | Quest Nichols Institute – Valencia, CA. Please provide SERVICE AREA INFORMATION to find available tests you can order.

Clinical Significance

See available Test Resources

Test Resources

Test FAQ
XSense®, Fragile X with Reflex and Chromosome Analysis, Blood

Algorithm
Laboratory Evaluation of Developmental Delay/Intellectual Disability (DD/ID)

Includes

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Methodology

Screen: Polymerase Chain Reaction (PCR) with Detection by Capillary Electrophoresis • Culture • Microscopy • Karyotype
Reflex: Methylation PCR

Assay Category

This test was developed and its analytical performance characteristics have been determined by Quest Diagnostics. It has not been cleared or approved by FDA. This assay has been validated pursuant to the CLIA regulations and is used for clinical purposes.

Reference Range(s)

See Laboratory Report

Alternative Name(s)

Fragile X with Reflex,Fragile X Syndrome (FXS),Martin-Bell Syndrome,Fra (X),FMR1,FRAX

LOINC® Codes, Performing Laboratory

Service Area must be determined

Preferred Specimen(s)

10 mL whole blood

Minimum Volume

5 mL

Collection Instructions

Whole blood: Normal phlebotomy procedure. Specimen stability is crucial. Store and ship room temperature immediately. Collect whole blood in sodium heparin (green-top) tube. Do not transfer whole blood to M4. **Do not refrigerate or freeze.**

Transport Container

Sodium heparin (green-top) tube

Transport Temperature

Room temperature

Specimen Stability

Room temperature: See individual tests
Refrigerated: See individual tests
Frozen: Unacceptable

Reject Criteria

Received frozen

Setup Schedule

Service Area must be determined