Fragile X Syndrome Testing Brochure

quadrant laboratories

Fragile X Syndrome

Fragile X syndrome (FXS) testing detects more than 99% of individuals (both males and females) with FXS, as well as premutation carriers of the condition.

Related Gene(s): FMR1

What is fragile X syndrome?

Fragile X syndrome is a genetic disorder affecting approximately 1 in 1250 males and 1 in 2000 females[1,2]. It is the most common cause of inherited intellectual disability and developmental delay in males[3]. Typically, males with fragile X syndrome are more severely affected than females and present a spectrum of neurodevelopmental disorders including learning disabilities, cognitive impairment, and autism spectrum disorder (ASD)[4].

American Academy of Pediatrics (AAP) recommends that any child who presents with developmental delay, borderline intellectual abilities, or mental retardation or has a diagnosis of autism without a specific etiology should undergo molecular testing for fragile X syndrome. The American College of Obstetricians and Gynecologists (ACOG) and the American College of Medical Genetics (ACMG) recommend that carrier screening for fragile X syndrome be offered to women with a family history of fragile X syndrome or undiagnosed intellectual disability before or during pregnancy. In addition, ACOG recommends that screening be offered to women with a family history of developmental delay, autism, or premature ovarian insufficiency. Carrier screening for fragile X syndrome may be considered for any woman before or during pregnancy.

Given the possibility of a link, it is recommended that all children with autism, both male and female, be referred for genetic testing for FXS and any other genetic cause of autism.

What are the common features of fragile X syndrome?

Affected children usually have delayed development of speech and language by 2 years of age. Most males have mild to moderate intellectual disability, while about one-third of affected females with fragile X syndrome are intellectually disabled. Children may also have anxiety, hyperactive behaviors, and attention deficit disorder (ADD). This includes an impaired ability to maintain attention and difficulty focusing on specific tasks. About one-third of individuals with fragile X syndrome have features of Autism. Seizures occur in about 15 percent of males and about 5 percent of females with fragile X syndrome[5].

Most males and about half of females with fragile X syndrome have features that become more apparent with age[5]. The physical features include a long and narrow face, large ears, a prominent jaw and forehead, unusually flexible fingers, flat feet, and in males, enlarged testicles (macroorchidism) after puberty.

What is the genetic cause for fragile X syndrome?

Fragile X syndrome is caused by changes in the FMR1 gene, which is located on the X chromosome. In most cases, it is caused by expansion of the trinucleotide CGG repeat in the 5' untranslated region of the FMR1 gene.

What do the results mean?

The Quadrant Laboratories Fragile X Repeat Assay uses the tri-primer PCR (polymerase chain reaction) and capillary electrophoresis (CE) technologies to detect the CGG repeat size(s) in the FMR1 gene.

The FMR1 gene not only causes fragile X syndrome but a spectrum of conditions called fragile X-related disorders (such as FXTAS and POI) depending on the CGG repeat size and gender.

Normal individuals have between 2-44 copies of the CGG repeat. However, in some individuals, the number of trinucleotide repeat units is increased to between 55 and 200, known as a premutation carrier. Females carrying a premutation are at risk for their allele to expand to a full mutation and may have fragile X-tremor/ataxia syndrome (FXTAS) and primary ovarian insufficiency (POI). Individuals with a full mutation have more than 200 repeats. Males carrying full mutations are usually affected with FXS. Females are variably affected. Alleles between 44 and 55 repeats are intermediate such that some alleles are stable and some are unstable. To date, no allele with fewer than 56 repeats has been reported to expand to a full mutation in a single generation[5,6,7].

Who should be tested for fragile X?

Individuals may be tested by their doctor for fragile X syndrome and associated disorders including:

- Men or women with intellectual or developmental delay, and/or autism, especially if they have any physical or behavioral characteristics of fragile X syndrome.
- A family history of fragile X syndrome, or a male or female relative with undiagnosed intellectual disability.
- Any women who are having reproductive or fertility problems associated with early ovarian insufficiency or early menopause.
- Adults over 50 with features of fragile X associated tremors (FXTAS), who have intention tremor or ataxia (problems with balance).

Other Resources:

The National Fragile X Foundation is an organization created to support families with fragile X-associated disorders. • www.FragileX.org

FRAXA Research Foundation is a resource for families to receive educational materials, guidance, and other fragile X associated resources. • www.FRAXA.org

Related Tests:

- Autism Spectrum Disorder (ASD) NGS Panel
- Array CGH (a-CGH)

Specimen Requirements

Saliva/Oral Swab

Saliva specimens are accepted when a test is ordered through a physician with a valid National Provider Identifier (NPI).

Ordering Information

Please include the following completed and signed forms with each sample:

- Test requisition form
- Informed consent
- Letter of Medical Necessity

Shipping

Samples should be kept at room temperature. Do not freeze specimens. Please follow specific instructions provided in the collection kit.

Turnaround Time: 3-4 weeks

Contact us for more information:
Email: support@quadrantlaboratories.com
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References:

1. Chen, H. (2016). Fragile X Syndrome. In: Atlas of Genetic Diagnosis and Counseling. Springer, New York, NY. https://doi.org/10.1007/978-1-4614-6430-3_96-2
2. Webb, T. (1989). The epidemiology of the fragile X syndrome. In K. E. Davis (Ed.), The fragile X syndrome (pp. 40–55). Oxford: Oxford University Press.
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5. https://medlineplus.gov/genetics/condition/fragile-x-syndrome/
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