PREMIER GENOMICS

FRAGILE X SYNDROME GENETIC SCREENING

Fragile X syndrome is the most common form of inherited intellectual disability.

It affects approximately 1 in 3,600 males and 1 in 6,000 females. Fragile X syndrome (FXS) is caused by an expansion of a repeated region of the promoter of the *FMR1* gene on the X chromosome. FXS occurs when an individual has more than 200 copies of the repeated region of this gene—or a full mutation.[1]

Characteristics of Premutation and Fragile X Syndrome[1-6]

Premutation

- One-third of men over age 50 with a premutation will develop problems with:
  - Balance
  - Memory
  - Tremors

Full mutation (FXS)

- Intellectual disability
- Loose connective tissue
- Distinctive facial features
- Autism
- Behavioral issues

Premutation

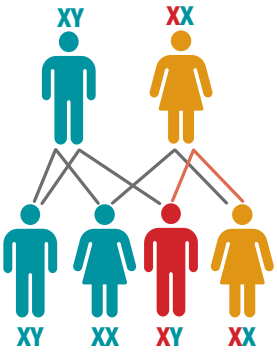
- 5% to 10% of women over age 50 with a premutation will develop problems with:
  - Balance
  - Memory
  - Tremors
- 20% of women with a premutation may experience:
  - Early menopause
  - Fertility problems
- Thyroid issues
- Muscle pain

Full mutation (FXS)

- Mild to borderline intellectual disability
- Shyness and anxiety

Males inherit their X chromosome from their mothers; therefore, a father with FXS or a premutation cannot transmit this to their sons. If a mother has a premutation, it may expand to a full mutation in her male or female children.

Fragile X Syndrome Inheritance*



- Affected by Fragile X Syndrome
- Carrier of Fragile X Syndrome
- Not affected by Fragile X Syndrome

X Fragile X chromosome
X Normal X chromosome
Y Normal Y chromosome

*This is a normal X-linked inheritance pattern. In this case, one of the mother's X chromosomes has a full mutation. She will be symptomatic.

ACOG and ACMG Fragile X Syndrome Screening Recommendations[1,7]

Consider screening pregnant patients, or those considering pregnancy, who present with *any* of the following:

X	Family history of fragile X syndrome
X	Personal and/or family history of undiagnosed intellectual disability
X	Personal and/or family history of autism
X	Personal and/or family history of ovarian insufficiency
X	Personal history of elevated follicle-stimulating hormone
X	Personal history of a premutation

Abbreviations: ACOG, American Congress of Obstetricians and Gynecologists; ACMG, American College of Medical Genetics and Genomics.

Actionable Fragile X Syndrome Genetic Screening Results

Category	CGG Repeats	Risk	Consideration
Normal	<45	Patient is not a carrier for the most common alteration in the *FMR1* gene and is not at risk for having a child with FXS.	N/A
Intermediate	45-54	Patient's results fall between "normal" and "premutation." Patient is not at risk for having a child with FXS. Future generations may be at risk for FXS.	Small chance that child is at risk for premutation; future generations should be screened for FXS
Premutation	55-200	Patient is a carrier of the altered *FMR1* gene. Women may be at risk for early menopause and fertility problems. Men and women are at increased risk for later onset tremor, as well as balance and memory problems. Patient is at risk for having a child with FXS.	Consider carrier screening; prenatal diagnostic testing is available
Full mutation	>200	Patient is a carrier of the altered *FMR1* gene. Patient is at risk for having a child with FXS.	Prenatal diagnostic testing is available

PREMIER GENOMICS

FRAGILE X SYNDROME GENETIC SCREENING

FRAGILE X SYNDROME GENETIC TESTING PROCESS

THE PROCESS	The DNA collection process is simple, and requires only an in-office buccal (cheek) swab with our sample collection kit. UPS will pick up your patient samples and deliver them directly to our lab (labels and instructions are included in each kit). Dedicated account services are always available to answer questions and manage requests.
THE TURN-AROUND TIME	7 to 10 days
THE REPORT	Upon completion of DNA extraction and evaluation at our advanced laboratory facility, a comprehensive report is generated and uploaded to a secure portal with dedicated physician log-in and downloading capabilities. Physician-to-physician consultation is also available with our Medical Director or our Genetic Counselor. Monograph is available upon request.

Talk to your representive or visit our web site for our full catalog of genetic testing solutions.
Personalized Genetic Medicine // Inherited Genetic Disorders // Women's Genetic Health

ABOUT PREMIER GENOMICS

Premier Genomics is committed to advancing the field of personalized genetic medicine by offering cutting-edge genetic screening services to help practitioners and their patients in pursuit of tailored treatment and optimized, personalized health care. We work together with patients and their insurance providers to help ensure that access to these important genetic tests does not cause patients financial hardship.

PREMIER GENOMICS

Premier Genomics | www.PremierGx.com | dnatest@premiergx.com
250 Ed English Drive, Building 3, Unit D, Shenandoah, TX 77385
CLIA-accredited, CAP-certified clinical laboratory

References: 1. American Congress (formerly College) of Obstetricians and Gynecologists (ACOG) Committee on Genetics. ACOG Committee Opinion No. 469: Carrier screening for fragile X syndrome. *Obstet Gynecol.* 2010;116(4):1008-1010. **2.** Seltzer MM, Baker MW, Hong J, Maenner M, Greenberg J, Mandel D. Prevalence of CGG expansions of the *FMR1* gene in a US population-based sample. *Am J Med Genet B Neuropsychiatr Genet.* 2012;159B(5):589-597. **3**. Chonchaiya W, Schneider A, Hagerman RJ. Fragile X: a family of disorders. *Adv Pediatr.* 2009:56:165-186. **4.** Saul RA, Tarleton JC. *FMR1*-related disorders. In: Pagon RA, Adam MP, Ardinger HH, et al, eds. *GeneReviews.* Seattle, WA: University of Washington, Seattle; 2012. http://www.ncbi.nlm.nih.gov/books/NBK1384/. Posted June 16, 1998. Updated April 26, 2012. Accessed December 29, 2015. **5.** Coffey SM, Cook K, Tartaglia N, et al. Expanded clinical phenotype of women with the *FMR1* premutation. *Am J Med Genet A.* 2008;146A(8):1009-1016. **6.** Rodriguez-Revenga L, Madrigal I, Pagonabarraga J, et al. Penetrance of *FMR1* premutation associated pathologies in fragile X syndrome families. *Eur J Hum Genet.* 2009;17(10):1359-1362. **7.** Sherman S, Pletcher BA, Driscoll DA. American College of Medical Genetics and Genomics (ACMG) Practice Guideline: Fragile X syndrome: diagnostic and carrier testing. *Genet Med.* 2005;7(8):584-587.