Molecular Diagnostic Laboratory
Phone: (314) 454-8685
FAX: (314) 454-7616

Jacqueline Payton, MD, PhD, FCAP
Medical Director
http://pathology.wustl.edu/patientcare/moldiagnostic.ph

Fragile X-associated Tremor/ Ataxia Syndrome (FXTAS)

Measuring CGG trinucleotide repeat expansions of the *FMR1* gene

Indications for Molecular Testing

- Adult (>50 y.o.) onset of tremor and/or neurological disorders including progressive tremor, gait ataxia, and cognitive decline
- A family history of Fragile X Syndrome, or male or female relatives with undiagnosed mental retardation.

Testing Methodology

Screening procedure utilizes Polymerase Chain Reaction (PCR). If unable to determine fragment sizes by PCR, then direct mutation testing is performed by Southern analysis (Methylation). Southern analysis involves determination of restriction endonuclease DNA fragment sizes and methylation status with the StB12.3 *FMR1* probe. Patients at risk for FXTAS do not exhibit symptoms of Fragile X Syndrome.

Interpretation of DNA analysis

FXTAS is distinct from Fragile X syndrome, the most common cause of inherited mental retardation. However, both conditions arise as a consequence of a CGG trinucleotide repeat expansion in the *FMR1* gene. The number of CGG repeats varies from 6 to approximately 40 in normal alleles. Premutations have between approximately 55 and 200 CGG repeats. Males with a premutation do not typically display characteristics of fragile X syndrome and usually have a normal IQ. Those who eventually develop FXTAS are generally over 50 years of age. Men with FXTAS may be misdiagnosed as having Parkinson disease, Alzheimer disease, or senile dementia. The estimated incidence of FXTAS is 1 in 3000 males over the age of 50 in the general population (up to 30% of male carriers with a fragile X premutation), with increasing penetrance with increasing age [17% of men aged 50 – 59 years, 38% of 60 - 69 yrs, 50% of 70 -79 yrs, and 75% of 80-89 yrs (ref 2)]. This is less frequent than the 1 to 5% of older adults who develop essential tremor but is similar to the 1 in 2000 prevalence of late-onset ataxia. Screening programs suggest that >5% of sporadic ataxia among older adult males may be attributable to FXTAS. Female premutation carriers may also develop FXTAS or, more commonly, Premature Ovarian Syndrome (POF).

Specimen Requirements

Peripheral blood--1 lavender-top (EDTA) tube (3cc). Invert several times to mix blood. Do not freeze. Forward promptly at ambient temperature to the following address:

Molecular Diagnostic Laboratory
Barnes-Jewish Hospital, Institute of Health
Mail Stop 90-28-344
425 South Euclid Avenue, Room 5970
St. Louis, MO 63110

Clinical information must be provided with specimen referral in order to correctly interpret test results.

Current Pricing

Contact Lab Customer Service for current pricing 314 362-1470.
CPT codes: PCR 81243, Southern analysis (additional) 81244

OSHU DNA Diagnostic Lab, Version 4 protocol
Tassone F, Pan R, Amiri K, Taylor AK, Hagerman PJ. A rapid polymerase chain reaction-based screening method for identification of all expanded alleles of the fragile X (FMR1) gene in newborn and high-risk populations. J Mol Diagn. 2008;10:43-9.
Spector EB, Kronquist K, et al. Technical Standards and Guidelines for Fragile X Testing by the American College of Medical Genetics. 2006. Electronic publication available at: http://www.acmg.net/pages/acmg_activities/stds-2002/fx.htm
Hamdan H, Tynan J, Fenwick R, Leo J. Automated detection of trinucleotide repeats in Fragile X syndrome. Molecular Diagnosis 4 December 1997;2(4):259-269.
Warren ST, Nelson DL. Advances in Molecular Analysis of Fragile X syndrome. JAMA 16 February 1994;271(7):536-542.
Jacquemont S., Hagerman R., Leehey M., Hall D., Levine R. Penetrance of the Fragile X-Associated Tremor/Ataxia Syndrome in a Premutation Carrier Population. JAMA, January 28, 2004, 291 (4): 460-469.