Informed Consent for FMR1 Fragile X Testing

Please read the following form carefully and discuss with your ordering physician/genetic counselor before signing consent.

1. This is a genetic (DNA-based) test using PCR, and if necessary, Southern Blot to test for expansion of the CGG repeat in the 5’ untranslated region of the Fragile X gene (FMR1).

2. The purpose of this analysis is to test for Fragile X-syndrome, an X-linked form of hereditary mental retardation; for fragile X tremor ataxia syndrome (FXTAS); or to explain premature ovarian failure.

2a. You (or the person for whom you are signing) may want genetic counseling before signing consent.

3. This is a test for genetic susceptibility ("genetic predisposition"), the risk of having the disorder may be altered by family history and/or other factors. If the test is positive for the disorder or for an increased risk of the disorder, you may wish to have further independent testing, consult your physician or have genetic counseling.

4. The condition being tested for is Fragile X syndrome, or its carrier state.

5. A male positive for a full mutation will almost certainly exhibit features of Fragile X syndrome; in a symptomatic adult, a premutation supports a diagnosis of FXTAS; a female who is positive for a full mutation may or may not have Fragile X syndrome; a woman who tests for a premutation may develop early menopause and may exhibit features of FXTAS; in addition, there is a 50% chance of passing on the abnormal premutation allele to her children with a 3% to 100% chance of expansion to a full mutation (depending upon the size of the premutation allele). A negative result makes the above conditions unlikely (but does not exclude them). Approximately 1% of cases of FMRI-associated mental retardation are due to mutations that cannot be detected by this test.

6. The results of the above test become a part of the patient’s medical record, and may be made available to individuals/organizations with legal access to the patient’s medical record, on a strict “need-to-know” basis, including but not limited to the physicians and nursing staff directly involved in the patient’s care, the patient’s current and future insurance carriers, and other specifically authorized by the patient/authorized representative to gain access to the patient’s medical records.

7. No additional tests will be performed on this sample, without specific, signed authorization by the patient. After 60 days, unless consent is given the sample will be destroyed – please see below.

8. Medicare/Insurance Carriers may not pay for the test, in which case, the patient/responsible party will be billed for the test.

Person obtaining consent:

_____________________________________________________       ________________________________________________________________  Date: _____________________
Print Name of Person Obtaining Consent
Signature of Person Obtaining Consent

I have read and fully understood the above, and give my consent for this testing.

Patient (person being tested):

_____________________________________________________       ________________________________________________________________  Date: _____________________
Print Name of Patient/Authorized Representative
Signature of Patient/Authorized Representative

Relationship to Patient: _________________________________________________

Consent for Sample Retention:

☐ I do not consent to research. My blood may be used for routine laboratory use only.

☐ I consent to possible future genetic research on my blood if all identifying information is removed (name, address, date of birth, medical record number). The duration of the retention of my blood sample will depend on the individual research study. If the blood is not used in a study, it will be destroyed or anonymously used as described above.

☐ I consent to the use of my specimen in research on developmental diseases. I have signed/shall sign an IRB approved informed consent for study __________________. Please forward my specimen to the PI __________________ who shall be responsible for ensuring that the specimen is used in accordance with the IRB protocol.
Note to health care practitioner obtaining consent to test for Fragile-X syndrome.

It is New York State Law that all genetic testing requires informed consent. Please ensure that the patient understands the contents of the informed consent and prior to signature. Expansion of CGG repeats in the 5’ Untranslated region of the first exon of the FMR1 gene with resulting methylation of the region and loss of expression of its RNA and encoded protein causes greater than 99% of cases of Fragile-X syndrome the most common cause of hereditary mental retardation in males. Testing for FMR1 can be a predictive or diagnostic test for Fragile X.

The test estimates the number of CGG repeats in the 5’ untranslated region of the first exon of the FMR1 gene by measuring the size of a PCR product that includes this region. A second PCR using a primer complementary to the CGG repeat can detect most expanded alleles that do not amplify with the first primer pair, although the exact size of larger expansions may not be determined. In addition, there is a chance that some very large expansions may be missed. Furthermore, in some males with expanded alleles, some cells may have a premutation allele and others a full mutation allele (see definition below). Therefore, DNA from males with a large premutation, females with only one detected allele, and all patients with an expanded allele whose size cannot be determined will be retested utilizing a Southern Blot assay that determines the size and methylation status of the alleles.

Definitions

Normal alleles: Approximately 5-40 repeats. Alleles of this size are stably transmitted without any increase or decrease in repeat number.

Mutable normal alleles: Intermediate alleles (also termed "gray zone"). No consensus exists on the precise definition, but the recommendation of the updated 2006 technical guidelines of the American College of Medical Genetics, recommend that it be defined as 41-54.

Premutation alleles: Approximately 55-200 repeats. Alleles of this size are not associated with mental retardation but are associated with Fragile X Tremor Ataxia Syndrome (FXTAS) and Premature Ovarian Failure. Women with alleles in this range are at risk for having children with full mutations. The risk of expansion of a transmitted premutation allele to a full mutation increases from 3% for alleles in the 55-59 repeat range, to virtually 100% for alleles over 90 repeats.

Full mutation alleles: More than 200 repeats, with several hundred to several thousand repeats being typical. These alleles show aberrant hypermethylation with resulting loss of expression. These alleles are associated with Fragile X syndrome in males, and may be associated with variable degrees of mental retardation in females.

Indications

Fragile X syndrome:
• Individuals of either sex with mental retardation, developmental delay, or autism, especially if they have (a) any physical or behavioral characteristics of fragile X syndrome, (b) a family history of fragile X syndrome, or (c) male or female relatives with undiagnosed mental retardation.
• Individuals seeking reproductive counseling who have (a) a family history of fragile X syndrome or (b) a family history of undiagnosed mental retardation.

Ovarian dysfunction:
• Women who are experiencing reproductive or fertility problems associated with elevated follicle stimulating hormone (FSH) levels, especially if they have (a) a family history of premature ovarian failure, (b) a family history of fragile X syndrome, or (c) male or female relatives with undiagnosed mental retardation. Note that some women with premature ovarian failure will show alleles in the high normal range. There may be a continuous gradation of risk.

Tremor/ataxia syndrome:
• Men and women who are experiencing late onset intention tremor and cerebellar ataxia of unknown origin, especially if they have (a) a family history of movement disorders, (b) a family history of fragile X syndrome, or (c) male or female relatives with undiagnosed mental retardation.

Sample Requirements and Shipping: Please obtain an informed consent, note the specific indication, both the patient/person signing for the patient, and the licensed practitioner obtaining the consent should sign the consent form. Collect at least 2 ml of EDTA-anticoagulated blood (purple top), and transport at room temperature (do not freeze) to the Molecular Pathology Laboratory at the address indicated on the informed consent. The sample should reach the laboratory within 72 hours.