LASTNAME, FIRSTNAME

Patient ID:

Specimen ID: **000-000-0000-0**

DOB: **mm/dd/yyyy**

Age: **00**

Sex: **Female**

Account Number: **00000000**

Ordering Physician:

labcorp

Date Collected: **mm/dd/yyyy** | Date Received: **mm/dd/yyyy** | Date Reported: **mm/dd/yyyy** | Date Entered: **mm/dd/yyyy**

Specimen Type: **Whole Blood**

Ethnicity: **Not Provided**

Indication: **Not Provided**

Fragile X Syndrome, Diagnostic

SAMPLE REPORT

Summary: ■ POSITIVE

Variants Detected

Disorder *(Gene)*	Result	Interpretation
Fragile X syndrome *(FMR1)* NM_002024.5	POSITIVE: PREMUTATION CARRIER PCR: 30 and 56 Premutation allele AGG interruption(s): 1 Haplotype:(CGG)25 AGG (CGG)31	Premutation carrier of fragile X syndrome. Risk of expansion to full mutation in offspring is <1% (Domniz, PMID:30619448). This individual may be at risk for primary ovarian insufficiency and late-onset fragile X-associated tremor/ataxia syndrome (FXTAS), and for having children with fragile X syndrome. Genetic counseling is recommended.

Recommendations

Genetic counseling is recommended to discuss the potential clinical and/or reproductive implications of positive results, as well as recommendations for testing family members and, when applicable, this individual's partner. Genetic counseling services are available. To access Labcorp Genetic Counselors please visit https://womenshealth.labcorp.com/genetic-counseling or call (855) GC-CALLS (855-422-2557).

Additional Clinical Information

Fragile X syndrome is an X-linked disorder of intellectual disability with variable severity. Expansions of CGG repeat sequences in the *FMR1* gene account for 99% of variants causing fragile X syndrome. The risk of expansion from a premutation allele of 55-90 repeats to a full mutation in offspring, when transmitted by a carrier female, is reduced with increasing number of AGG interruptions in the CGG repeat sequence (Yrigollen, PMID:22498846; Nolin, PMID:25210937). Greater than 99% of males and approximately 50% of females with the full mutation are intellectually disabled. Other signs and symptoms may include delayed speech and language skills, autism, hyperactivity, developmental delay, increased susceptibility to seizures, macroorchidism in males, a long, narrow face with prominent ears, and joint laxity. Individuals with a premutation do not have fragile X syndrome, but may have an increased risk for fragile X-related disorders. Females may have fragile X-associated primary ovarian insufficiency (FXPOI), which can cause infertility or early menopause. Most males with a premutation and some females are at risk for fragile X-associated tremor and ataxia syndrome (FXTAS), which can affect balance and is associated with tremor and memory problems in older individuals. Treatment is supportive and focuses on educational and behavioral support and management of symptoms. (Santoro, PMID:22017584).

Comments

This interpretation is based on the clinical information provided and the current understanding of the molecular genetics of the disorder(s) tested. Information about the disorder(s) tested is available at https://womenshealth.labcorp.com.

Methods/Limitations

Fragile X Syndrome: PCR analysis is used to detect the number of CGG repeats on each allele of the *FMR1* gene. The reportable range is 5-200 repeats. Alleles with expansions above 200 repeats are reported as >200. In females, excluding prenatal specimens, alleles between 55 and 90 repeats are assessed by a PCR assay to determine the number and position of AGG interruptions within the CGG repeats. If indicated, methylation status is determined by PCR analysis based on methylation-specific immunoprecipitation. Interpretation of repeat expansion results is based on the following ranges: Negative: < 45 repeats; intermediate: 45-54 repeats; premutation: 55-200 repeats; full mutation: >200 repeats. The analytical sensitivity of this assay for the detection of expanded alleles in the *FMR1* gene is estimated to be >99%. Reproducibility of repeat numbers is typically ±1 for alleles containing up to 60 repeats, ±3 for alleles with 61-119 repeats, and ±10 for alleles with >119 repeats. Low levels of mosaicism (<5%) and *FMR1* variants unrelated to trinucleotide expansion are not detected by this assay.

Limitations: Technologies used do not detect germline mosaicism and do not rule out the presence of large chromosomal aberrations including rearrangements and gene fusions, or variants in regions or genes not included in this test, or possible inter/intragenic interactions between variants, or repeat expansions. Variant classification and/or interpretation may change over time if more information becomes available. False positive or false negative results may occur for reasons that include: rare genetic variants, sex chromosome abnormalities, pseudogene interference, blood transfusions, bone marrow transplantation, somatic or tissue-specific mosaicism, mislabeled samples, or erroneous representation of family relationships.

References

Hunter JE, Berry-Kravis H, *et al*., FMR1 Disorders. 1998 Jun16 (Updated 2019 Nov 21). In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews®[Internet]. PMID: 20301558

Electronically released by Director1 WB

Fragile X Syndrome, Diagnostic

References (Cont.)

Spector E, Behlmann A, Kronquist K, *et al*. Laboratory testing for fragile X, 2021 revision: a technical standard of the American College of Medical Genetics and Genomics (ACMG). *Genet Med* 23, 799 (2021). PMID: 33795824

Performing Labs

Component Type	Performed at	Laboratory Director
Technical component, processing	Esoterix Genetic Laboratories, LLC, 3400 Computer Drive, Westborough, MA 01581-1771	Hui Zhu, PhD, FACMG
Technical component, analysis	Esoterix Genetic Laboratories, LLC, 3400 Computer Drive, Westborough, MA 01581-1771	Hui Zhu, PhD, FACMG
Professional component	Esoterix Genetic Laboratories, LLC, 3400 Computer Drive, Westborough, MA 01581-1771	Hui Zhu, PhD, FACMG

For inquiries, the physician may contact the lab at 800-255-7357

This test was developed and its performance characteristics determined by Esoterix Genetic Laboratories, LLC. It has not been cleared or approved by the Food and Drug Administration.

Esoterix Genetic Laboratories, LLC is a subsidiary of Laboratory Corporation of America Holdings, using the brand Labcorp.

Patient Details
LASTNAME, FIRSTNAME

Phone:
Date of Birth: **mm/dd/yyyy**
Age: **00**
Sex: **Female**
Patient ID:
Alternate Patient ID:

Physician Details
CLIENT NAME
CLIENT ADDRESS

Phone: **000000000**
Account Number: **00000000**
Physician ID:
NPI:

Specimen Details
Specimen ID: **00000000000**
Control ID:
Alternate Control Number:
Date Collected: **mm/dd/yyyy 0000 Local**
Date Received: **mm/dd/yyyy 1428 ET**
Date Entered: **mm/dd/yyyy 1201 ET**
Date Reported: **mm/dd/yyyy 1703 ET**

Electronically released by Director1 WB