Integrated GENETICS
LabCorp Specialty Testing Group

SAMPLE REPORT

Fragile X Analysis
PCR with Reflex Southern Blot

Patient Name: LASTNAME, FIRSTNAME
Referring Physician:
Specimen #: **Client #:**
Patient ID: **Case #:**

CLIENT ADDRESS

DOB: MM/DD/YYYY
Sex: F
SSN: ***-**-****

Date Collected: MM/DD/YYYY
Date Received: MM/DD/YYYY
Lab ID:
Hospital ID:
Specimen Type: **BLDPER**

Indication: Carrier test / Screening

RESULTS: Southern: 2.8, 3.0, 5.2 and 5.4 kb. PCR: 30 and 76 repeats

INTERPRETATION
Premutation carrier of fragile X syndrome. Premutation allele has 1 AGG interruption: (CGG)9 AGG (CGG)66. Risk of expansion to full mutation in offspring is 40% (Domniz, PMID:30619448). This individual may be at risk for primary ovarian insufficiency (POI), late-onset fragile X-associated tremor/ataxia syndrome (FXTAS), and for having children with fragile X syndrome. Genetic counseling is recommended. See Comments.

COMMENTS:
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 mutations causing fragile X syndrome. The interpretation is based on the following ranges of repeat sequences:

Negative:	<45 repeats
Intermediate:	45-54 repeats
Premutation:	55-200 repeats with normal methylation pattern
Full Mutation:	>200 repeats with abnormal methylation pattern

The risk for a premutation allele of 55-90 repeats to expand 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).

This interpretation is based on the clinical and family relationship information provided and the current understanding of the molecular genetics of this condition. Genetic counseling is recommended for any individual seeking additional information regarding interpretation of genetic test results.

Under the direction of:

(REPORT CONTINUED ...)

Date Reported:

DIRECTOR NAME

Testing Performed At Esoterix Genetic Laboratories, LLC, 3400 Computer Drive Westborough, MA 01581 Bernice A. Allitto, PhD, FACMG, Laboratory Director 800-255-7357

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METHOD / LIMITATIONS:
DNA is amplified by the polymerase chain reaction (PCR) to determine the size of the CGG repeat region within the FMR1 gene. PCR products are generated using a fluorescence labeled primer and sized by capillary gel electrophoresis. If indicated, Southern blot analysis is performed by hybridizing the probe StB12.3 to EcoRI- and EagI-digested DNA. The analytical sensitivity of both Southern blot and PCR analyses is 99% for expansion mutations in the FMR1 gene. Reported CGG repeat sizes may vary as follows: +/- one for repeats less than 60, and +/- two to four for repeats in the 60 - 120 range. For repeats greater than 120, the accuracy is +/- 10%. If 55-90 trinucleotide repeats are detected in females (excluding prenatal specimens), a PCR assay targeting AGG sequences within the CGG repeats is performed to assess the number and position of AGG interruptions.

REFERENCES: Garber K et al. Eur J Hum Genet 2008;16:666-72. Rodriguez-Revenga L et al. Eur J Hum Genet 2009:1-4. Sherman S et al. Genet Med 2005;7:584-87. Wittenberger MD et al. Fertil Steril 2007;87:456-65.

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