LASTNAME, FIRSTNAME

Patient ID:

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

DOB: **mm/dd/yyyy**

Age: **00**

Sex: **Female**

Account Number: **00000000**

Ordering Physician:

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: **Carrier Test / Screening**

Inheritest® Core Panel

3 genes

SAMPLE REPORT

Summary: ■ POSITIVE

Variants Detected

Disorder *(Gene)*	Result	Interpretation
Spinal muscular atrophy *(SMN1)* NM_000344.3	POSITIVE: CARRIER 1 copy of *SMN1*.	Predicted to be a carrier. **Risk:** AT INCREASED RISK FOR AFFECTED PREGNANCY. If this individual's reproductive partner is also a carrier the risk for an affected fetus is 25%. Genetic counseling and reproductive partner carrier screening is recommended.

Negative Results

Disorder *(Gene)*	Result	Interpretation
Cystic fibrosis *(CFTR)* NM_000492.3	NEGATIVE	This result reduces, but does not eliminate, the risk to be a carrier. **Risk:** NOT at an increased risk for an affected pregnancy.
Fragile X syndrome *(FMR1)* NM_002024.5	NEGATIVE PCR: 29 and 29	Not a carrier of a fragile X expansion. **Risk:** NOT at an increased risk for an affected pregnancy.

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

Spinal muscular atrophy (SMA) is an autosomal recessive neurodegenerative disorder with variable age at onset and severity, characterized by progressive degeneration of the lower motor neurons in the spinal cord and brain stem, leading to muscle weakness, and in its most common form, respiratory failure by age two. Complications of SMA may include poor weight gain, sleep difficulties, pneumonia, scoliosis, and joint deformities. In severely affected individuals, abnormal fetal ultrasound findings may include congenital joint contractures, polyhydramnios, and decreased fetal movement. (Korinthenberg, PMID:9307259). Treatment is supportive. Targeted therapies may be available for some individuals. Approximately 94% of affected individuals have 0 copies of the *SMN1* gene; in these individuals, an increase in the number of copies of the *SMN2* gene correlates with reduced disease severity (Feldkotter M, PMID:11791208). Individuals with one copy of the *SMN*1 gene are predicted to be carriers of SMA; those with two or more copies have a reduced carrier risk. For individuals with two copies of the *SMN1* gene, the presence or absence of the variant c.*3+80T>G correlates with an increased or decreased risk, respectively, of being a silent carrier (2+0).

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

Next-generation Sequencing: Genomic regions of interest are selected using the Twist Biosciences® hybridization capture method and sequenced via the Illumina® next generation sequencing platform. Sequencing reads are aligned with the human genome reference GRCh37/hg19 build. Regions of interest include coding exons, intron/exon junctions (+/- 20 nucleotides) and additional genomic regions with known significant pathogenic variants. Analytical sensitivity at 30X coverage is estimated to be >99% for single nucleotide variants, >99% for insertions/deletions less than six base pairs and >96% for insertions/deletions between six and forty-five base pairs. Regions with low NGS coverage are selected for Sanger sequencing based on analytical sensitivity and probability of pathogenic variant(s). Qiagen CLC Genomics and in-house algorithms identify copy number variants (CNVs) by comparing normalized read depth for each target in the region of interest with a set of clinical control samples. Expected minimum size resolution for CNVs in *CFTR* and *DMD* is 200 bp. For all other genes, expected minimum size resolution for CNVs is 1000 bp. Precise breakpoints are not reported.

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Methods/Limitations (Cont.)

Single-exon deletions or duplications are not detected in some cases due to the CNV size limitations, or due to isolated data quality variation or intrinsic sequence properties. Confirmatory testing by orthogonal technologies includes Sanger sequencing, MLPA, gap PCR and low coverage whole genome sequencing analysis.

If the following genes are included in this test, these analysis restrictions are applied: *F2* includes one variant: c.*97G>A (also known as 20210G>A); *F5* includes the F5 Leiden c.1601G>A (p.Arg543Gln) (also known as R506Q) variant only; *CORO1A* excludes exon 11; *GJB2* analysis includes deletions involving the 5' end of *GJB6* and regulatory elements of *GJB2,* which result in reduced *GJB2* expression; *HFE* includes five variants: c.187C>G (p.His63Asp), c.502G>T (p.Glu168X), c.506G>A (p.Trp169X), c.845G>A (p.Cys282Tyr), and c.1006+1G>A; *NEB* excludes exons 82-105.

The following regions may have lower analytical sensitivity due to intrinsic sequence properties: *ACAT1* exon 2, *ATP6V1B1* exon 1, *BBS9* exon7, *BRIP1* exon 17, *CRLF1* exon1, *GBE1* exon5, *HGSNAT* exon 1, *IDUA* exon1, *LIFR* exons 15 and 19, *PKHD1* exon 43, *PTPRC* exon 15, *SELENON* exons 1 and 3.

Reported variants: Pathogenic and likely pathogenic variants are reported for all tests. Benign and likely benign variants are typically not reported. Variants of uncertain significance are reported when included in the test specification. Variants are specified using the numbering and nomenclature recommended by the Human Genome Variation Society (HGVS, http://www.hgvs.org/). Variant classification and confirmation are consistent with ACMG standards and guidelines (Richards, PMID:25741868; Rehm, PMID:23887774). Detailed variant classification information and reevaluation are available upon request.

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.

Spinal muscular atrophy: The copy number of *SMN1* exon 7 is assessed relative to internal standard reference genes by quantitative polymerase chain reaction (qPCR). A mathematical algorithm calculates 0, 1, 2 and 3 copies with statistical confidence. In fetal specimens and specimens with 0 or 1 copies, the primer and probe binding sites are sequenced to rule out variants that could interfere with copy number analysis. *SMN2* copy number is assessed by digital droplet PCR analysis relative to an internal standard reference gene in samples with no copies of *SMN1*. For carrier screening, when two copies of *SMN1* are detected, allelic discrimination qPCR targeting c.*3+80T>G in *SMN1* is performed.

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

Gregg AR, Aarabi M, Klugman S *et al*. Screening for autosomal recessive and X-linked conditions during pregnancy and preconception: a practice resource of the American College of Medical Genetics and Genomics (ACMG). *Genet Med* 23, 1793 (2021). PMID: 34285390

Disorders Tested

Cystic fibrosis (1 gene). Autosomal recessive: *CFTR*
Fragile X syndrome (1 gene). X-linked: *FMR1*. Males are not tested for X-linked disorders.
Spinal muscular atrophy (1 gene). Autosomal recessive: *SMN1*

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

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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.

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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 1426 ET**
Date Entered: **mm/dd/yyyy 1153 ET**
Date Reported: **mm/dd/yyyy 1654 ET**

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