

Specimen ID:  
Control ID:

Acct #:

Phone:

# SAMPLE REPORT

**Patient Details**

DOB: 00/00/0000  
Age (yyy/mm/dd): 000/00/00  
Gender: Female  
Patient ID: 00000000

**Specimen Details**

Date collected: 00/00/0000  
Date received: 00/00/0000  
Date entered: 00/00/0000  
Date reported: 00/00/0000

**Physician Details**

Ordering:  
Referring:  
ID:  
NPI:

Ethnicity: Ashkenazic Jewish  
Indication: DMD: Screening

Specimen Type: Whole Blood

Lab ID:

DISEASE (GENE)	RESULTS	INTERPRETATION
Dystrophinopathies, including Duchenne and Becker muscular dystrophies and dilated cardiomyopathy (DMD) NM 004006	NEGATIVE.	This result reduces, but does not eliminate, the chance to be a carrier. See Additional Clinical Information.

Genetic counseling services are available. To access Integrated Genetics Genetic Counselors please call (855) GC-CALLS (855-422-2557).

**ADDITIONAL CLINICAL INFORMATION**

**Dystrophinopathies, including Duchenne and Becker muscular dystrophies and dilated cardiomyopathy:** The dystrophinopathies are X linked muscle disorders with variable severity that include Duchenne muscular dystrophy (DMD), Becker muscular dystrophy (BMD) and X linked dilated cardiomyopathy. The dystrophinopathies are characterized by progressive muscle weakness and wasting and occur predominantly in males. Skeletal muscle is primarily affected in DMD and BMD. Heart muscle is primarily affected in X-linked dilated cardiomyopathy. Signs and symptoms of DMD and BMD may include large calves, unusual gait, difficulty running, climbing and getting up from the floor, problems with learning and memory, intellectual disability, progressive muscle weakness leading to wheelchair dependence before age 13 (DMD), or after age 16 (BMD), and cardiomyopathy. Individuals with DMD usually experience symptoms in early childhood and may live into their 20s. Individuals with BMD may have less severe symptoms with later onset and slower progression, and life expectancy into their 40s. Treatment is supportive and multidisciplinary. Genotype-targeted therapies may be available for some individuals. Approximately 10% of carrier females may be at risk for developing cardiomyopathy, mild muscle weakness, and/or cognitive problems. The dystrophinopathies are caused by pathogenic variants in the *DMD* gene. Approximately 67% of the time a *DMD* pathogenic variant is inherited, and approximately 33% of the time the variant is *de novo* and not previously seen in the family. If a pathogenic variant is *de novo*, the risk that the mother of an affected male has germline mosaicism is 15-20%. This analysis does not detect germline mosaicism. An individual who has a negative carrier screen may have germline mosaicism and be at risk for having an affected child.

**COMMENTS**

This interpretation is based on the clinical information provided and the current understanding of the molecular genetics of the disease(s) tested. References and additional information about the disorders tested are available at [www.integratedgenetics.com](http://www.integratedgenetics.com).

Under the direction of:

Testing performed at Esoterix Genetic Laboratories, LLC, 3400 Computer Drive, Westborough, MA 01581 Bernice A. Allitto, PhD, FACMG, Laboratory Director 1-800-255-7357

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## METHOD/LIMITATIONS

**Next generation sequencing (NGS):** Genomic regions of interest are selected using the Agilent®SureSelectXT® hybridization capture method for target enrichment 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 all exons and splice junctions for each gene analyzed. Targeted regions are sequenced to at least 200X mean base coverage with a minimum of 99% of bases at  $\geq 20X$  coverage. Analytical sensitivity is estimated to be  $>99\%$  for single nucleotide variants and small insertions/deletions ( $\leq 6$  bp).

**Alpha thalassemia:** Analysis of the alpha-globin (*HBA*) gene cluster is performed by multiplex ligation-dependent amplification (MLPA). Variants included in the analysis are the Constant Spring non-deletion variant and the following deletions:  $-\alpha 3.7$ ,  $-\alpha 4.2$ ,  $-\alpha 20.5$ ,  $-\alpha \text{SEA}$ ,  $-\alpha \text{FIL}$ ,  $-\alpha \text{THAI}$ ,  $-\alpha \text{MED}$ , and the HS-40 regulatory region. This MLPA analysis does not detect other variants in the alpha-globin genes or variants in the beta-globin gene and may not detect the co-occurrence of a deletion and a duplication. Analytical sensitivity is estimated to be  $>99\%$  for the targeted variants.

**Dystrophinopathies, including Duchenne and Becker muscular dystrophies and dilated cardiomyopathy:** Analysis is performed by NGS. A deletion or duplication of exons in the *DMD* gene is identified when  $>60\%$  of an exon has an aberrant copy number. In-frame and out-of-frame deletions cannot be distinguished by this analysis, which does not determine precise breakpoints in the *DMD* gene. Approximately 67% of the time a *DMD* pathogenic variant is inherited, and approximately 33% of the time the variant is *de novo* and not previously seen in the family. If a pathogenic variant is *de novo*, the risk that the mother of an affected male has germline mosaicism is 15-20%. This analysis does not detect germline mosaicism. An individual who has a negative carrier screen may have germline mosaicism and be at risk for having an affected child.

**Reported variants:** Pathogenic and likely pathogenic variants and variants of uncertain significance (VUS) are reported after confirmation by Sanger sequencing or an appropriate technology. Non-deletion variants are specified using the numbering and nomenclature recommended by the Human Genome Variation Society (HGVS, <http://www.hgvs.org/>). Benign variants are not reported. Variant classification is consistent with ACMG standards and guidelines (Richards, PMID:25741868). Detailed variant classification information is available upon request. A variant of uncertain significance (VUS) should not be used in clinical decision making; a VUS is classified based on inadequate or conflicting evidence regarding its pathogenicity or clinical relevance.

**Limitations:** Technologies used do not detect germline mosaicism, and do not rule out the presence of large chromosomal aberrations, including rearrangements, or variants in regions or genes not included in this test, or possible inter/intragenic interactions between variants. Variant classification and/or interpretation may change over time if more information becomes available. False positive or negative results may occur for reasons that include: 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.

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.

Integrated Genetics is a business unit of Esoterix Genetic Laboratories, LLC, a wholly-owned subsidiary of Laboratory Corporation of America Holdings.

Under the direction of:

Testing performed at Esoterix Genetic Laboratories, LLC, 3400 Computer Drive, Westborough, MA 01581 Bernice A. Allitto, PhD, FACMG, Laboratory Director 1-800-255-7357