SAMPLE REPORT

Specimen ID: 00000000
Control ID:

Acct #:
Phone:

LASTNAME, FIRSTNAME

CLIENT ADDRESS

Patient Details
DOB: M/DD/YYYY
Age (yyy/mm/dd): YYY/MM/DD
Gender: Female
Patient ID: 00000000

Specimen Details
Date collected: M/DD/YYYY 00:00 AM
Date received: M/DD/YYYY 00:00 PM
Date entered: M/DD/YYYY 00:00 PM
Date reported: M/DD/YYYY 00:00 PM

Physician Details
Ordering: ORDERING PHYS. NAME
Referring:
ID:
NPI:

Ethnicity: Not Provided
Indication: not provided

Specimen Type: Whole Blood

Lab ID:

DISORDER *(GENE)*	RESULTS	INTERPRETATION
Dystrophinopathies, including Duchenne and Becker muscular dystrophies and dilated cardiomyopathy *(DMD)*	POSITIVE. Heterozygous for a pathogenic deletion of all or part of exon(s) 1-3	Predicted to be at least a carrier. Female carriers may be at risk for symptoms, including X-linked dilated cardiomyopathy. Genetic counseling is recommended. See Additional Clinical Information.
Spinal muscular atrophy *(SMN1)*	NEGATIVE	2 copies of *SMN1*; negative for c.*3+80T>G SNP. This result reduces, but does not eliminate the risk to be a carrier. For ethnic-specific risk revisions see Information Table.
Fragile X syndrome *(FMR1)*	PCR: 30 and 31 repeats.	Negative: not a carrier of a fragile X expansion mutation. This result is not associated with fragile X syndrome.
All other disorders	NEGATIVE for the mutations analyzed.	These results reduce, but do not eliminate, the chance to be a carrier. See Information Tables.

All Inheritest carrier screening panels include disorders for which professional societies have provided guidelines, including cystic fibrosis and spinal muscular atrophy. Genetic counseling services are available. To access Integrated Genetics Genetic Counselors please visit www.integratedgenetics.com/genetic-counseling or 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

Under the direction of:

mosaicism. An individual who has a negative carrier screen may have germline mosaicism and be at risk for having an affected child. Genetic counseling is recommended to discuss the potential clinical and/or reproductive implications of these results, as well as recommendations for testing family members and, when applicable, this individual's partner. If a mutation in this gene is inherited by a male fetus, the male fetus is expected to be affected. If a mutation in this gene is inherited by a female fetus, the female fetus is expected to be at least a carrier. Females with mutations in X-linked conditions may have symptoms of the disorder.

Spinal muscular atrophy: 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, PMID:11791208). Individuals with one copy of the *SMN1* 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) (Luo, PMID 23788250; Feng, PMID 28125085).

Fragile X syndrome: 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. 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 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).

COMMENTS

This analysis provides carrier testing by analyzing 144 genes for more than 9,400 pathogenic variants associated with more than 115 autosomal recessive or X-linked disorders. Interpretations and risk calculations, where applicable, are based on the ethnic information and clinical and family relationships provided, as well as the current understanding of the molecular genetics of the conditions tested. Clinical sensitivity and specificity varies for each disease and for each ethnic group. References and additional information about the disorders are available at www.integratedgenetics.com.

The standard of care for Tay-Sachs disease carrier detection in all ethnic groups is enzyme (hexosaminidase A) analysis. For maximum sensitivity and specificity, enzyme analysis should be performed in addition to DNA variant analysis (Schneider, PMID:19876898). If Tay-Sachs enzyme analysis was ordered, results are reported separately.

The standard of care for determining carrier status for sickle cell disease and other hemoglobinopathies is to combine information from clinical assessment, complete blood count, hemoglobin electrophoresis, and DNA testing (Traeger-Synodinos, PMID:25052315). If hemoglobin electrophoresis was ordered, results are reported separately.

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

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. Targeted regions are sequenced to at least 200X mean base coverage with a minimum of 99% of bases at ≥20X coverage. Analytical sensitivity is estimated to be >99% for single nucleotide variants and small insertions/deletions (≤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: −alpha3.7, −alpha4.2, −−alpha20.5, −−SEA, −−FIL, −−THAI, −−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.

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. When no copies of *SMN1* are detected, the primer and probe binding sites are sequenced to rule out variants that could interfere with copy number analysis and *SMN2* copy number is assessed by digital droplet PCR analysis relative to an internal standard reference gene. For carrier screening, when two copies of *SMN1* are detected, allelic discrimination qPCR targeting c.*3+80T>G in *SMN1* is performed.

Fragile X syndrome: 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.

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

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 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.

Under the direction of:

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Patient: **Specimen ID:**
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INFORMATION TABLES

SMA risk reductions for individuals with no family history						
Disorder (*Gene*) Reference sequence	**Population**	**Detection rate (Copy number + SNP)**	**Pre-test carrier risk**	**Post-test risk for being a carrier with 2 copies****		**Post-test risk of being a carrier with 3 copies**
				POSITIVE for the c.*3+80T>G SNP	**NEGATIVE for the c.*3+80T>G SNP**	
Spinal muscular atrophy (*SMN1*) NM_000344	African American	90.3%	1 in 72	1 in 34	1 in 375	1 in 4200
	Ashkenazi Jewish	92.8%	1 in 67	High risk	1 in 918	1 in 5400
	Asian	93.6%	1 in 59	High risk	1 in 907	1 in 5600
	Caucasian	95.0%	1 in 47	1 in 29	1 in 921	1 in 5600
	Hispanic	92.6%	1 in 68	1 in 140	1 in 906	1 in 5400
	Mixed or other ethnic background	For counseling purposes, consider using the ethnic background with the most conservative risk estimate				

** includes carriers who are silent carriers (2+0) and carriers with a pathogenic variant not detected in this assay
Feng, PMID 28125085; Luo, PMID 23788250; Sugarman, PMID 21811307

Gene-specific risk reductions for individuals with no family history				
Disorder (*Gene*) Reference sequence	**Population**	**Detection Rate**	**Pre-test carrier risk**	**Post-test carrier risk with negative result**
Abetalipoproteinemia (*MTTP*) NM_000253	Ashkenazi Jewish	N/A*	N/A	N/A
Adenosine deaminase deficiency (*ADA*) NM_000022	General	42%	1 in 289	1 in 497
Alpha-mannosidosis (*MAN2B1*) NM_000528	Caucasian	63%	1 in 350	1 in 944
Alpha-thalassemia (*HBA1, HBA2*) 16p13.3	African American Eastern Mediterranean European Southeast Asian Western Pacific	90% 90% 90% 90% 90% 90%	1 in 2 1 in 21 1 in 5 1 in 44 1 in 2 1 in 10	N/A N/A N/A N/A N/A N/A
Alport syndrome, COL4A3-related (*COL4A3*) NM_000091	Ashkenazi Jewish	95%	1 in 183	1 in 3640
Andermann syndrome (*SLC12A6*) NM_133647	French Canadian	99%	1 in 23	1 in 2200
Argininosuccinic aciduria (*ASL*) NM_000048	Finnish Worldwide	86% 59%	1 in 190 1 in 132	1 in 1350 1 in 320
Arthrogryposis, mental retardation, and seizures (AMRS) (*SLC35A3*) NM_012243	Ashkenazi Jewish	N/A*	N/A	N/A
Aspartylglucosaminuria (*AGA*) NM_000027	Finnish	98%	1 in 81	1 in 4000

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Disorder (*Gene*) Reference sequence	Population	Detection Rate	Pre-test carrier risk	Post-test carrier risk with negative result
Ataxia with vitamin E deficiency (*TTPA*) NM_000370	Italian North African	80% 99%	N/A* N/A*	N/A N/A
Ataxia-telangiectasia (*ATM*) NM_000051	Amish Costa Rican North African Jewish Norwegian Worldwide	99% 56% 97% 55% 40%	N/A* 1 in 100 1 in 81 1 in 197 1 in 100	N/A 1 in 226 1 in 2667 1 in 436 1 in 166
Autosomal recessive spastic ataxia of Charlevoix-Saguenay (ARSACS) (*SACS*) NM_014363	French Canadian	96%	1 in 21	1 in 500
Bardet-Biedl syndrome, BBS1-related (*BBS1*) NM_024649	Worldwide	55%	1 in 390	1 in 865
Bardet-Biedl syndrome, BBS2-related (*BBS2*) NM_031885	Ashkenazi Jewish	N/A*	1 in 136	N/A
Bardet-Biedl syndrome, BBS10-related (*BBS10*) NM_024685	Worldwide	45%	1 in 418	1 in 759
Beta hemoglobinopathy, beta thalassemias (*HBB*) NM_000518	African American East Asian Mediterranean Middle Eastern South Asian Southeast Asian	90% 93% 97% 84% 95% 90%	1 in 75 1 in 50 1 in 20 1 in 30 1 in 20 1 in 30	1 in 741 1 in 700 1 in 634 1 in 182 1 in 381 1 in 291
Beta hemoglobinopathy, hemoglobins C, D, E, and O (*HBB*) NM_000518	African American Asian Asian Indian Middle Eastern Native American Southeast Asian	>99% >99% >99% >99% >99% >99%	1 in 46 1 in 119 1 in 68 1 in 255 1 in 292 1 in 15	Negligible Negligible Negligible Negligible Negligible Negligible
Beta hemoglobinopathy, sickle cell disease (*HBB*) NM_000518	African American Hispanic Middle Eastern Native American	>99% >99% >99% >99%	1 in 14 1 in 183 1 in 360 1 in 176	Negligible Negligible Negligible Negligible
Beta-mannosidosis (*MANBA*) NM_005908	Worldwide	81%	N/A*	N/A
Bloom syndrome (*BLM*) NM_000057	Ashkenazi Jewish	97%	1 in 134	1 in 4434
Canavan disease (*ASPA*) NM_000049	Ashkenazi Jewish	98%	1 in 55	1 in 2700
Carbamoyl phosphate synthetase I deficiency (*CPS1*) NM_001875	Worldwide	48%	1 in 570	1 in 1095
Carnitine palmitoyltransferase II deficiency (*CPT2*) NM_000098	Caucasian	72%	N/A*	N/A
Carnitine-acylcarnitine translocase deficiency (*SLC25A20*) NM_000387	Worldwide	N/A*	N/A	N/A
Cartilage-hair hypoplasia (*RMRP*) NM_003051	Amish Finnish Worldwide	91% 92% 48%	1 in 19 1 in 76 N/A*	1 in 200 1 in 938 N/A

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Disorder (*Gene*) Reference sequence	Population	Detection Rate	Pre-test carrier risk	Post-test carrier risk with negative result
Citrullinemia type I (*ASS1*) NM_000050	Japanese Worldwide	71% 52%	N/A* 1 in 119	N/A 1 in 247
Cobalamin C disease (*MMACHC*) NM_015506	Worldwide	89%	N/A*	N/A
Cohen syndrome (*VPS13B*) NM_017890	Finnish Worldwide	75% 54%	N/A* N/A*	N/A N/A
Congenital amegakaryocytic thrombocytopenia (*MPL*) NM_005373	Ashkenazi Jewish	95%	1 in 75	1 in 1480
Congenital disorder of glycosylation type 1a (*PMM2*) NM_000303	Caucasian	89%	1 in 71	1 in 637
Cystic fibrosis (*CFTR*) NM_000492	African American Ashkenazi Jewish Asian American Caucasian Hispanic	>81% >97% >55% >93% >78%	1 in 61 1 in 24 1 in 94 1 in 25 1 in 58	1 in 316 1 in 767 1 in 208 1 in 343 1 in 260
Cystinosis (*CTNS*) NM_004937	French Canadian Worldwide	70% 61%	1 in 39 1 in 158	1 in 127 1 in 403
D-bifunctional protein deficiency (*HSD17B4*) NM_000414	Worldwide	51%	N/A*	N/A
Dihydrolipoamide dehydrogenase deficiency (*DLD*) NM_000108	Ashkenazi Jewish	95%	1 in 107	1 in 2121
Dihydropyrimidine dehydrogenase deficiency (*DPYD*) NM_000110	Northern European Caucasian	71%	N/A*	N/A
Dystrophinopathies, includes Duchenne and Becker muscular dystrophies and cardiomyopathies (*DMD*) NM_004006	Worldwide	95%	N/A**	N/A
Ehlers-Danlos syndrome type VIIC (*ADAMTS2*) NM_014244	Ashkenazi Jewish Worldwide	95% 80%	N/A* N/A*	N/A N/A
Ethylmalonic encephalopathy (*ETHE1*) NM_014297	Mediterranean/Arab	61%	N/A*	N/A
Familial dysautonomia (*IKBKAP*) NM_003640	Ashkenazi Jewish	99%	1 in 31	1 in 3000
Familial hyperinsulinism, ABCC8-related (*ABCC8*) NM_000352	Ashkenazi Jewish Finnish	97% 43%	1 in 52 1 in 101	1 in 1700 1 in 175
Familial Mediterranean fever (*MEFV*) NM_000243	Arab Armenian Ashkenazi Jewish North African Jewish Turkish	71% 78% 69% 94% 74%	1 in 5 1 in 5 1 in 81**** 1 in 7 1 in 5	1 in 14 1 in 19 1 in 259 1 in 100 1 in 16
Fanconi anemia group C (*FANCC*) NM_000136	Ashkenazi Jewish	99%	1 in 100	1 in 9900
Fucosidosis (*FUCA1*) NM_000147	Worldwide	80%	N/A*	N/A
Galactosemia, GALT-related (*GALT*) NM_000155	African American Ashkenazi Jewish Caucasian	65% 88% 81%	1 in 78 1 in 127 1 in 108	1 in 221 1 in 1050 1 in 564
Galactosialidosis (*CTSA*) NM_000308	Japanese	60%	N/A*	N/A

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Disorder (*Gene*) Reference sequence	Population	Detection Rate	Pre-test carrier risk	Post-test carrier risk with negative result
Gaucher disease (*GBA*) NM_001005741	Ashkenazi Jewish	98%	1 in 15	1 in 700
Glutaric acidemia type 1 (*GCDH*) NM_000159	Amish German	94% 55%	1 in 9 1 in 158	1 in 134 1 in 350
Glutathione synthetase deficiency (*GSS*) NM_000178	Worldwide	67%	N/A*	N/A
Glycine encephalopathy, AMT-related (*AMT*) NM_000481	Worldwide	50%	N/A*	N/A
Glycine encephalopathy, GLDC-related (*GLDC*) NM_000170	Finnish	70%	1 in 117	1 in 387
Glycogen storage disease type Ia (*G6PC*) NM_000151	Ashkenazi Jewish Worldwide	99% 81%	1 in 64 1 in 177	1 in 6300 1 in 927
Glycogen storage disease type Ib (*SLC37A4*) NM_001164277	Worldwide	46%	1 in 354	1 in 654
Glycogen storage disease type III (*AGL*) NM_000642	Faroese North African Jewish Worldwide	99% 99% 85%	1 in 30 1 in 37 1 in 159	1 in 2900 1 in 3600 1 in 1054
GM1 gangliosidosis and mucopolysaccharidosis type IVB (*GLB1*) NM_000404	Worldwide	45%	1 in 160	1 in 290
GRACILE syndrome (*BCS1L*) NM_004328	Finnish	99%	1 in 110	1 in 10,900
Guanidinoacetate methyltransferase deficiency (*GAMT*) NM_000156	Portuguese Worldwide	83% 68%	1 in 125 N/A*	1 in 730 N/A
Hereditary fructose Intolerance (*ALDOB*) NM_000035	Worldwide	75%	1 in 71	1 in 281
HMG-CoA lyase deficiency (*HMGCL*) NM_000191	Saudi Arabian Spanish/Portuguese	86% 85%	N/A* N/A*	N/A N/A
Holocarboxylase synthetase deficiency (*HLCS*) NM_000411	Worldwide	66%	1 in 158	1 in 463
Homocystinuria, CBS-related (*CBS*) NM_000071	United States	65%	1 in 227	1 in 647
Hypophosphatasia, autosomal recessive (*ALPL*) NM_000478	Japanese Mennonite	55% 99%	N/A* 1 in 25	N/A 1 in 2400
Joubert syndrome 2 (*TMEM216*) NM_001173990	Ashkenazi Jewish	99%	1 in 92	1 in 9100
Junctional epidermolysis bullosa, LAMA3-related (*LAMA3*) NM_000227	Pakistani	99%	N/A*	N/A
Junctional epidermolysis bullosa, LAMB3-related (*LAMB3*) NM_000228	Worldwide	55%	1 in 418	1 in 927
Junctional epidermolysis bullosa, LAMC2-related (*LAMC2*) NM_005562	Italian	29%	1 in 425	1 in 598
Krabbe disease (*GALC*) NM_000153	Caucasian	60%	1 in 158	1 in 393

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Disorder (*Gene*) Reference sequence	Population	Detection Rate	Pre-test carrier risk	Post-test carrier risk with negative result
Leigh syndrome, autosomal recessive (*FOXRED1, NDUFAF2, NDUFS4, NDUFS7, NDUFV1, COX15, SURF1*) NM_017547, NM_174889, NM_002495, NM_024407, NM_007103, NM_004376, NM_003172	Worldwide	30%	1 in 100	1 in 142
Leigh syndrome, French Canadian type (*LRPPRC*) NM_133259	French Canadian	98%	1 in 23	1 in 1100
Long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency (LCHAD) (*HADHA*) NM_000182	Dutch Worldwide	87% 71%	1 in 158 1 in 138	1 in 1208 1 in 473
Maple syrup urine disease type 1A (*BCKDHA*) NM_000709	Mennonite	99%	1 in 13	1 in 1200
Maple syrup urine disease type 1B (*BCKDHB*) NM_183050	Ashkenazi Jewish	95%	1 in 97	1 in 1921
Medium-chain acyl-CoA dehydrogenase deficiency (MCAD) (*ACADM*) NM_000016	United States	79%	1 in 63	1 in 296
Metachromatic leukodystrophy (*ARSA*) NM_000487	Caucasian Japanese	56% 50%	1 in 141 1 in 132	1 in 319 1 in 263
Methylmalonic acidemia, MMAA-related (*MMAA*) NM_172250	Caucasian	80%	1 in 300	1 in 1496
Methylmalonic acidemia, MMAB-related (*MMAB*) NM_052845	Caucasian	70%	1 in 435	1 in 1448
Methylmalonic acidemia, MUT-related (*MUT*) NM_000255	African American Hispanic	59% 63%	1 in 195 1 in 195	1 in 474 1 in 525
Mitochondrial acetoacetyl-CoA thiolase deficiency (*ACAT1*) NM_000019	Vietnamese Worldwide	94% 65%	N/A* N/A*	N/A N/A
Mucolipidosis type II and III, GNPTAB-related (*GNPTAB*) NM_024312	French Canadian Worldwide	99% 79%	1 in 39 1 in 152	1 in 3800 1 in 720
Mucolipidosis type IV (*MCOLN1*) NM_020533	Ashkenazi Jewish	96%	1 in 89	1 in 2200
Mucopolysaccharidosis type I (*IDUA*) NM_000203	Caucasian Japanese Scandinavian	60% 42% 79%	1 in 158 1 in 158 1 in 158	1 in 393 1 in 271 1 in 748
Mucopolysaccharidosis type II (*IDS*) NM_000202	Worldwide	44%	N/A**	N/A
Mucopolysaccharidosis type IIIA (*SGSH*) NM_000199	Worldwide	70%	1 in 170	1 in 564
Mucopolysaccharidosis type IIIB (*NAGLU*) NM_000263	Dutch Worldwide	73% 42%	1 in 244 1 in 220	1 in 901 1 in 379
Mucopolysaccharidosis type IIIC (*HGSNAT*) NM_152419	Worldwide	67%	N/A*	N/A
Mucopolysaccharidosis type IIID (*GNS*) NM_002076	Worldwide	62%	N/A*	N/A
Mucopolysaccharidosis type IVA (*GALNS*) NM_000512	General	49%	1 in 250	1 in 489
Mucopolysaccharidosis type VI (*ARSB*) NM_000046	Worldwide	42%	1 in 250	1 in 430

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Disorder (*Gene*) Reference sequence	Population	Detection Rate	Pre-test carrier risk	Post-test carrier risk with negative result
Mucopolysaccharidosis type VII (*GUSB*) NM_000181	Worldwide	48%	N/A*	N/A
Multiple sulphatase deficiency (SUMF1) NM_182760	Ashkenazi Jewish	N/A*	N/A	N/A
Nemaline myopathy, NEB-related (*NEB*) NM_001271208	Ashkenazi Jewish	95%	1 in 168	1 in 3341
Nephrotic syndrome, NPHS1-related (*NPHS1*) NM_004646	Finnish Maltese	94% 99%	1 in 45 1 in 22	1 in 734 1 in 2100
Nephrotic syndrome, NPHS2-related (*NPHS2*) NM_014625	Worldwide	60%	N/A*	N/A
Neuronal ceroid-lipofuscinosis, CLN3-related (*CLN3*) NM_001042432	General	85%	1 in 230	1 in 1527
Neuronal ceroid-lipofuscinosis, CLN5-related (*CLN5*) NM_006493	Finnish	99%	1 in 115	1 in 11,400
Neuronal ceroid-lipofuscinosis, CLN8-related (*CLN8*) NM_018941	Finnish	99%	1 in 135	1 in 13,400
Neuronal ceroid-lipofuscinosis, PPT1-related (*PPT1*) NM_000310	Finnish General	98% 57%	1 in 67 1 in 480	1 in 3300 1 in 1114
Neuronal ceroid-lipofuscinosis, TPP1-related (*TPP1*) NM_000391	General	53%	1 in 250	1 in 530
Niemann-Pick disease type C, NPC1-related (*NPC1*) NM_000271	Worldwide	31%	1 in 183	1 in 265
Niemann-Pick disease types A and B (*SMPD1*) NM_000543	Ashkenazi Jewish Worldwide	97% 40%	1 in 116 1 in 250	1 in 3834 1 in 416
Niemann-Pick disease type C, NPC2-related (*NPC2*) NM_006432	Worldwide	56%	1 in 866	1 in 1966
Nijmegen breakage syndrome (*NBN*) NM_002485	Eastern European Slavic	99%	1 in 177	1 in 17,600
Ornithine transcarbamylase deficiency (*OTC*) NM_000531	Worldwide	50%	N/A**	N/A
Phenylalanine hydroxylase deficiency, includes phenylketonuria (PKU) (*PAH*) NM_000277	Caucasian Irish Turkish	57% 69% 55%	1 in 50 1 in 33 1 in 26	1 in 114 1 in 104 1 in 56
Phosphoglycerate dehydrogenase deficiency, PHGDH-related (*PHGDH*) NM_006623	Ashkenazi Jewish	N/A*	N/A	N/A
Polycystic kidney disease, autosomal recessive (*PKHD1*) NM_138694	Finnish Worldwide	79% 59%	1 in 70 1 in 70	1 in 329 1 in 169
Pompe disease (*GAA*) NM_000152	African American Chinese Dutch	43% 80% 64%	1 in 60 1 in 112 1 in 100	1 in 104 1 in 556 1 in 276
Primary hyperoxaluria type 1 (*AGXT*) NM_000030	Worldwide	46%	1 in 289	1 in 534
Primary hyperoxaluria type 2 (*GRHPR*) NM_012203	Asian Caucasian	50% 58%	N/A* N/A*	N/A N/A
Propionic acidemia, PCCA-related (*PCCA*) NM_000282	Japanese	70%	1 in 65	1 in 214

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

Patient: **Specimen ID:**
DOB: **Patient ID:** **Control ID:** **Date collected:**

Disorder (*Gene*) Reference sequence	Population	Detection Rate	Pre-test carrier risk	Post-test carrier risk with negative result
Propionic acidemia, PCCB-related (*PCCB*) NM_000532	Caucasian Japanese Latin American Spanish	32% 77% 91% 68%	1 in 112 1 in 65 1 in 112 1 in 112	1 in 164 1 in 279 1 in 1234 1 in 338
Pyruvate dehydrogenase deficiency, PDHA1-related (*PDHA1*) NM_000284	Worldwide	40%	N/A**	N/A
Retinitis pigmentosa 59 (*DHDDS*) NM_024887	Ashkenazi Jewish	95%	1 in 322	1 in 6420
Rhizomelic chondrodysplasia punctata type 1 (*PEX7*) NM_000288	Worldwide	72%	1 in 158	1 in 561
Salla disease (*SLC17A5*) NM_012434	Finnish	96%	1 in 200	1 in 4976
Sandhoff disease (*HEXB*) NM_000521	Italian	75%	N/A*	N/A
Sialidosis (*NEU1*) NM_000434	Chinese Worldwide	89% 49%	N/A* N/A*	N/A N/A
Sjogren-Larsson syndrome (*ALDH3A2*) NM_000382	Swedish	87%	1 in 200	1 in 1531
Smith-Lemli-Opitz syndrome (*DHCR7*) NM_001360	Worldwide	75%	1 in 71	1 in 281
Sulfate transporter-related osteochondrodysplasias, includes achondrogenesis type 1B, atelosteogenesis type 2, diastrophic dysplasia, and recessive multiple epiphyseal dysplasia (*SLC26A2*) NM_000112	Finnish General	96% 70%	1 in 50 1 in 158	1 in 1226 1 in 524
Systemic primary carnitine deficiency (*SLC22A5*) NM_003060	Worldwide	43%	1 in 130	1 in 227
Tay-Sachs disease (*HEXA*) NM_000520	Ashkenazi Jewish US French Canadian Worldwide	96%*** 47%*** 46%***	1 in 27*** 1 in 73*** 1 in 300***	1 in 650 1 in 136 1 in 554
Tyrosinemia type 1 (*FAH*) NM_000137	Ashkenazi Jewish Finnish French Canadian Worldwide	99% 95% 95% 72%	1 in 158 1 in 122 1 in 56 1 in 158	1 in 15,700 1 in 2421 1 in 1100 1 in 562
Usher syndrome type IF (*PCDH15*) NM_033056	Ashkenazi Jewish	75%	1 in 147	1 in 585
Usher syndrome type IIIA (*CLRN1*) NM_174878	Ashkenazi Jewish Finnish	98% 98%	1 in 120 1 in 134	1 in 5951 1 in 6650
Very long-chain acyl-CoA dehydrogenase deficiency (VLCAD) (*ACADVL*) NM_000018	Worldwide	34%	1 in 222	1 in 336
Walker-Warburg syndrome, FKTN-related (*FKTN*) NM_001079802	Ashkenazi Jewish	99%	1 in 79	1 in 7800
Wilson disease (*ATP7B*) NM_000053	Asian Caucasian	39% 55%	1 in 50 1 in 90	1 in 81 1 in 199
Xeroderma pigmentosum, ERCC5-related (*ERCC5*) NM_000123	Worldwide	68%	N/A*	N/A

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Disorder (*Gene*) Reference sequence	Population	Detection Rate	Pre-test carrier risk	Post-test carrier risk with negative result
Xeroderma pigmentosum, XPA-related (*XPA*) NM_000380	Worldwide Japanese	91% 90%	N/A* 1 in 113	N/A 1 in 1120
Xeroderma pigmentosum, XPC-related (*XPC*) NM_004628	Tunisian Worldwide	99% 76%	1 in 50 N/A*	1 in 4900 N/A
X-linked severe combined Immunodeficiency (SCID) (*IL2RG*) NM_000206	Worldwide	68%	N/A**	N/A
Zellweger spectrum disorder, PEX10-related (*PEX10*) NM_153818	Worldwide	17%	1 in 646	1 in 778
Zellweger spectrum disorder, PEX12-related (*PEX12*) NM_000286	Worldwide	21%	1 in 373	1 in 472
Zellweger spectrum disorder, PEX1-related (*PEX1*) NM_000466	Worldwide	67%	1 in 134	1 in 404
Zellweger spectrum disorder, PEX26-related (*PEX26*) NM_017929	Worldwide	27%	1 in 646	1 in 885
Zellweger spectrum disorder, PEX2-related (*PEX2*) NM_000318	Ashkenazi Jewish	N/A*	1 in 123	N/A
Zellweger spectrum disorder, PEX6-related (*PEX6*) NM_000287	Worldwide	23%	1 in 280	1 in 363

* Not available: insufficient published data

** Not available: for this X-linked disorder carrier risk is different for males and females and cannot be obtained from observed incidence of the disorder as some female carriers are symptomatic

*** Excludes pseudodeficiency alleles

****The carrier frequency in healthy Ashkenazi Jewish individuals has been reported to be as high as 1 in 5; however, the carrier frequency of 1 in 81 is based on the observed incidence of the disorder

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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