Integrated GENETICS

SMN1 Copy Number Analysis

Patient Name: Donor 9896
DOB: [redacted] Age: [redacted]
SSN #: ***-**-**** Gender: Male

Specimen #: 62857166-1
Case #: 62749281 Patient ID #: 62392562
Date Collected: 07/02/2015 Date Received: 07/07/2015

803037 / 803038
Seattle Sperm Bank
4915 25th Avenue East
Suite 204W
Seattle, WA 98105
USA

Referring Physician: Jeffrey Olliffe
Genetic Counselor:

Specimen Type: Peripheral Blood

Clinical Data: Carrier Test/Gamete donor

Client Lab ID #:
Hospital ID #:
Specimen ID #:
Specimen(s) Received: 1 - Lavender 7 ml round bottom tube(s)
Ethnicity: Caucasian

RESULTS: SMN1 copy number: 2 (Reduced Carrier Risk)

INTERPRETATION:

This individual has an SMN1 copy number of two. This result reduces but does not eliminate the risk to be a carrier of SMA. Ethnic specific risk reductions based on a negative family history and an SMN1 copy number of two are provided in the Comments section of this report.

COMMENT:

Spinal muscular atrophy (SMA) is an autosomal recessive disease of variable age of onset and severity caused by mutations (most often deletions or gene conversions) in the survival motor neuron (SMN1) gene. Molecular testing assesses the number of copies of the SMN1 gene. Individuals with one copy of the SMN1 gene are predicted to be carriers of SMA. Individuals with two or more copies have a reduced risk to be carriers. (Affected individuals have 0 copies of the SMN1 gene.)

This copy number analysis cannot detect individuals who are carriers of SMA as a result of either 2 (or very rarely 3) copies of the SMN1 gene on one chromosome and the absence of the SMN1 gene on the other chromosome or small intragenic mutations within the SMN1 gene. This analysis also will not detect germline mosaicism or mutations in genes other than SMN1. Additionally, de novo mutations have been reported in approximately 2% of SMA patients.

Carrier Frequency and Risk Reductions for Individuals with No Family History of SMA				
Ethnicity	**Detection Rate[1]**	**Prior Carrier Risk[1]**	**Reduced Carrier Risk for 2 copy result**	**Reduced Carrier Risk for 3 copy result**
Caucasian	94.8%	1:47	1:834	1:5,600
Ashkenazi Jewish	90.5%	1:67	1:611	1:5,400
Asian	93.3%	1:59	1:806	1:5,600
Hispanic	90.0%	1:68	1:579	1:5,400
African American	70.5%	1:72	1:130	1:4,200
Asian Indian	90.2%	1:52	1:443	1:5,400
Mixed or Other Ethnic Background	For counseling purposes, consider using the ethnic background with the most conservative risk estimates.			

METHOD/LIMITATIONS: Specimen DNA is isolated and amplified by real-time polymerase chain reaction (PCR) for exon 7 of the SMN1 gene and the internal standard reference genes. A mathematical algorithm is used to calculate and report SMN1 copy numbers of 0, 1, 2 and 3. Based upon this analysis, an upper limit of 3 represents the highest degree of accuracy in reporting SMN1 copy number with statistical confidence. Sequencing of the primer and probe binding sites is performed on all fetal samples and samples with one copy of SMN1 by real-time PCR to rule out the presence of sequence variants which could interfere with analysis and interpretation. False positive or negative results may occur for reasons that include genetic variants, blood transfusions, bone marrow transplantation, erroneous representation of family relationships or contamination of a fetal sample with maternal cells.

REFERENCES:
1. Sugarman EA, Nagan N, Zhu H, et al. Pan-ethnic carrier screening and prenatal diagnosis for spinal muscular atrophy: clinical laboratory analysis of >72,400 specimens. Eur J Hum Genet 2012; 20:27-32. 2. Prior TW, et al. Technical standards and guidelines for spinal muscular atrophy testing. Genet Med 2011; 13(7): 686-694.

The test was developed and its performance characteristics have been determined by Esoterix Genetic Laboratories, LLC. The laboratory is regulated under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as qualified to perform high complexity clinical testing. This test must be used in conjunction with clinical assessment, when available. Integrated Genetics is a business unit of Esoterix Genetic Laboratories, LLC, a wholly-owned subsidiary of Laboratory Corporation of America Holdings.

Electronically Signed by: Zhaoqing Zhou, Ph.D., FACMG, on 07/16/2015
Reported by: /

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July 9, 2015

Seattle Sperm Bank
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SEATTLE, WA 98105

Test Results of: 9896, DONOR
DOB: [redacted] Sex: M
Collected on: 07/02/2015
Received on: 07/02/2015
Reported on: 07/09/2015

Patient ID#:

Branch Number: WAB55
Account Number: 46857540
Specimen Number: 183-129-0716-0
Specimen Type: Blood

Physician: OLLIFFE J

Test: Cystic Fibrosis, DNA Analysis

RESULTS: Negative for 32 mutations analyzed

INTERPRETATION:
This individual is negative for the mutations analyzed. This negative result may need further interpretation depending on the clinical indication. This result reduces but does not eliminate the risk to be a CF carrier.

COMMENTS:
The detection rate varies with ethnicity and is listed below. The presence of an undetected mutation in the CF gene cannot be ruled out. In the absence of family history, the remaining risk that a person with a negative result could have at least one CF mutation is listed in the table. If there is a family history of CF, these risk figures do not apply. As detailed information regarding this individual's family history would permit a more accurate assessment of this individual's risk to be a carrier of cystic fibrosis, please contact LabCorp Genetic Services at (800) 345-4363 for a revised report.

Mutation Detection Rates among Ethnic Groups	Detection rates are based on mutation frequencies in patients affected with cystic fibrosis. Among individuals with an atypical or mild presentation (e.g. congenital absence of the vas deferens, pancreatitis) detection rates may vary from those provided here:	
Ethnicity	**Carrier risk reduction when no family history**	**Detection Rate**
Ashkenazi Jewish	1/26 to 1/834	97%
Caucasian (non-Hispanic)	1/25 to 1/240	90%
African-American	1/65 to 1/207	69%
Hispanic	1/46 to 1/168	73%
Asian	1/94 to 1/208	55%

This interpretation is based on the clinical and family relationship information provided and the current understanding of the molecular genetics of this condition.

MUTATIONS ANALYZED:

G85E	A455E	S549N	R1162X	711+1 G→T	2184delA	3876delA
R117H	ΔI507	S549R	W1282X	1078delT	2789+5 G→A	3905insT
R334W	ΔF508	G551D	N1303K	1717-1 G→A	3120+1 G→A	
R347H	V520F	R553X	394delTT	1898+1 G→A	3659delC	
R347P	G542X	R560T	621+1 G→T	2183AA→G	3849+10kb C→T	

METHODS/LIMITATIONS:
DNA is isolated from the sample and tested for the 32 CF mutations on the Universal Array Platform (Luminex). Regions of the *CFTR* gene are amplified enzymatically and subjected to a solution-phase multiplex allele-specific primer extension with subsequent hybridization to a bead array and fluorescence detection. Polymorphisms F508C, I506V, and I507V are included in this panel to rule out false positive deltaF508 homozygotes. Reflex testing of 5T is included in the panel for R117H interpretation. False positive or negative results may occur for reasons that include genetic variants, blood transfusions, bone marrow transplantation, erroneous representation of family relationships or contamination of a fetal sample with maternal cells. The assay provides information intended to be used for carrier screening in adults of reproductive age, as an aid in newborn screening, and as a confirmatory test for another medically established diagnosis in newborns and children. The test is not intended for use in fetal diagnostic testing, pre-implantation screening, or for any stand-alone diagnostic purposes without confirmation by another medically established diagnostic product or procedure.

REFERENCES:

1. Updates on Carrier Screening for Cystic Fibrosis, (2011) Am J Ob Gynecol 117(4):1028-1031.
2. Watson, et al. (2004) *Genet Med* 6:387-91
3. Richards, et al. (2002) *Genet Med* 4:379-391
4. Preconception and prenatal carrier screening for cystic fibrosis: (2001)ACOG.ACMG publication

Results Released By: Melissa A. Hayden, Ph.D., Director
Report Released By: Melissa Hayden, Ph.D., Director

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Medical Director

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LabCorp Specialty Testing Group

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Seattle Sperm Bank

4915 25th Ave Ne Ste 204
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Ph: (206)588-1484
Fax: (206) 588-1485 WAB-55

LCLS Specimen Number: **183-129-0718-0**
Patient Name: **9896, DONOR**
Date of Birth: [redacted]
Gender: M
Patient ID:
Lab Number: (J15-2198 L

Account Number: 46857540
Ordering Physician: **J OLLIFFE**
Specimen Type: **BLOOD**
Client Reference: B0024827886
Date Collected: 07/02/2015
Date Received: 07/03/2015

Indications: DONOR TESTING

Date Reported: **07/13/2015**

Test: **Chromosome, Blood, Routine**

Cells Counted: 15
Cells Analyzed: 5

Cells Karyotyped: 2
Band Resolution: 550

CYTOGENETIC RESULT: 46,XY

INTERPRETATION: NORMAL MALE KARYOTYPE

Cytogenetic analysis of PHA stimulated cultures has revealed a MALE karyotype with an apparently normal GTG banding pattern in all cells observed.

This result does not exclude the possibility of subtle rearrangements below the resolution of cytogenetics or congenital anomalies due to other etiologies.

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[redacted]

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Specimen Type: **BLOOD**
Client Reference: B0024827886
Date Collected: 07/02/2015
Date Received: 07/03/2015

Hiba Risheg, PhD., FACMG
Board Certified Cytogeneticist

Patricia Kandalaft, MD
Medical Director
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National Director of Cytogenetics

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Professional Component performed by LabCorp/Dynacare CLIA 50D0632667, 550 17th Ave. Suite 200, Seattle WA 98122-5789. Medical Director, Patricia Kandalaft, MD
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July 7, 2015

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Test Results of: 9896, DONOR
DOB: [redacted] Sex: M
Collected on: 07/02/2015
Received on: 07/02/2015
Reported on: 07/07/2015

Branch Number: WAB55
Account Number: 46857540
Specimen Number: 183-129-0716-0
Specimen Type: Blood

Patient ID#:

Physician: OLLIFFE J

Test: Joubert Syndrome Type II

Result:

NEGATIVE
(No mutation identified)

Interpretation:
This individual is negative for the mutation analyzed. For detection rates and a revised carrier risk, see the table below.

Joubert Syndrome Type 2 (JBTS2, OMIM 608091) is an inherited, autosomal recessive early-onset disorder characterized by the absence or underdeveloped cerebellar vermis (an area of the brain that controls balance and coordination). This "molar tooth sign" can be seen on midbrain MRI. Common clinical findings in infants are abnormally rapid breathing, hypotonia, oculomotor apraxia/nystagmus, mental retardation, and an inability to coordinate voluntary muscle movements. Other findings include polydactyly, low set ears, small genitalia, high arched palate, and hepatic fibrosis. The disease has an elevated prevalence in the Ashkenazi Jewish population, with a carrier rate of 1 in 92. When both parents are carriers of JBTS2, there is a 1 in 4 (25%) chance with each pregnancy to have a child with the disease. Prenatal diagnosis is available.

Molecular genetic testing for JBTS2 encompasses one mutation in the *TMEM216* gene (11q12.2). Testing for the R12L (also called R73L) mutation identifies approximately greater than 99% of JBTS2 carriers in the Ashkenazi Jewish population. The carrier frequency in the non-Ashkenazi Jewish population has not been determined. A negative result decreases the likelihood that this person is a carrier, but cannot completely eliminate the possibility. The presence of a rare mutation cannot be ruled out. DNA test results must be combined with clinical information for the most accurate interpretation.

This table assumes no family history of Joubert Syndrome Type 2. Please call (800) 345-4363 for a revised report if this individual has a family history of JBTS2.

Ethnicity	Detection rate for the *TMEM216* mutation	Carrier risk prior to testing (assumes no family history)	Remaining risk given negative result
Ashkenazi Jewish	>99%	1/92	1/9101
Other	Not known	Not known	

Mutation:
R12L (R73L)

Methodology:
DNA analysis of the *TMEM216* gene (OMIM 613277) is performed on the Luminex Universal Array Platform using primer extension chemistry. Multiplex PCR amplifies DNA fragments containing the mutation above. Primer extension then generates a biotin-labeled product that hybridizes to complementary, bead-immobilized probes to permit flow-sorted detection of both normal and mutation sequences. Molecular-based testing is highly accurate, but as in any laboratory test, rare diagnostic errors may occur. This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary.

References:

1. Edvardson S, et al. 2010. Jourbert syndrome 2 (JTBS) in Ashkenazi Jews is associated with a *TMEM216* mutation. Am J Hum Genet. 86:93-97.

Results Released By: Melissa A. Hayden, Ph.D., Director
Report Released By: Melissa Hayden, Ph.D., Director

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Test Results of: 9896, DONOR
DOB: [redacted] Sex: M
Collected on: 07/02/2015
Received on: 07/02/2015
Reported on: 07/07/2015

Patient ID#:

Branch Number: WAB55
Account Number: 46857540
Specimen Number: 183-129-0716-0
Specimen Type: Blood

Physician: OLLIFFE J

Test: Gaucher disease, DNA Analysis

Result:

NEGATIVE
(No mutation identified)

Interpretation:
This individual is negative for the mutations analyzed. For detection rates and a revised carrier risk, see table below. If Gaucher Disease is a suspected diagnosis for this individual, enzyme analysis is recommended.

Gaucher Disease (Type 1, OMIM 230800) is an autosomal recessive disorder caused by a deficiency in the enzyme glucocerebrosidase. Deficient levels of glucocerebrosidase can result in visceral changes, such as organomegaly and thrombocytopenia, and skeletal changes, such as bone lesions. There are three subtypes of Gaucher Disease. Type 1 is the most common subtype. Individuals affected with Type 1 may have onset of symptoms in adolescence, though some remain asymptomatic well into adulthood. Type 1 is effectively treated through enzyme replacement therapy. Types 2 and 3 are rare and include onset in childhood and involve the central nervous system. The disease has an elevated prevalence among Ashkenazi Jewish individuals and non-Jewish Caucasian individuals, with a carrier frequency of 1 in 15 and 1 in 100, respectively. When both parents are carriers of Gaucher Disease, there is a 1 in 4 (25%) chance with each pregnancy to have a child with the disease. Prenatal diagnosis is available.

Molecular genetic testing for Gaucher Disease encompasses eight mutations in the glucocerebrosidase gene (*GBA*, 1q22). Testing for these mutations identifies 95% of Gaucher Disease carriers in the Ashkenazi Jewish population and 75% of the non-Jewish Causcasian carriers. A negative test result decreases the likelihood that a person is a carrier, but cannot completely eliminate the possibility. The presence of a rare mutation cannot be ruled out. DNA test results must be combined with enzyme test results and clinical information for the most accurate interpretation.

This table assumes no family history of Gaucher Disease. Please call (800) 345-4363 for a revised report if this individual has a family history of Gaucher Disease.

Ethnicity	Detection rate for Type 1 *GBA* mutations	Carrier risk prior to testing (assumes no family history)	Remaining risk given negative result
Ashkenazi Jewish	95%	1/15	1/281
non-Jewish, Caucasian	75%	1/100	1/397
Other	Not known	Not known	

Mutations:

N370S (A1226G)	L444P (C1448T)	D409H (G5957C)	V394L (5912T)
84GG (G-GG)	IVS2+1 G→A	R496H (G1604A)	55 bp deletion (C1263del)

Methodology:
DNA analysis of the glucocerebrosidase (*GBA*) gene (OMIM 606463) is performed on the Luminex Universal Array Platform using primer extension chemistry. Multiplex PCR amplifies DNA fragments containing the mutations above. Primer extension then generates a biotin-labeled product that hybridizes to complementary, bead-immobilized probes to permit flow-sorted detection of both normal and mutation sequences. Molecular-based testing is highly accurate, but as in any laboratory test, rare diagnostic errors may occur. This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary.

References:

1. Grabowski G. Genet Test (1997). 1(1):5-12.
2. Horowitz M, Pasmanik-Chor M, Borochowitz Z, et al. Hum Mutat (1998)12:240-4.
3. Beutler E, Gelbart T, West C. Genomics (1993) 15:203-5.
4. Gross SJ, Pletcher BA, Monaghan KG. Carrier screening in individuals of Ashkenazi Jewish descent. Genet Med 2008; 10(1):54-56.
5. Monaghan KG, Feldman GL, Palomaki GE, Spector EB, et al. Technical standards and guidelines for reproductive screening in the Ashkenazi Jewish population. Genet Med. 2008; 10(1):57-72.
6. American College of Obstetricians and Gynecologists, Committee Opinion. Washington, DC: ACOG; October 2009. #442

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July 7, 2015

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Test Results of: 9896, DONOR
DOB: [redacted] Sex: M
Collected on: 07/02/2015
Received on: 07/02/2015
Reported on: 07/07/2015

Branch Number: WAB55
Account Number: 46857540
Specimen Number: 183-129-0716-0
Specimen Type: Blood

Patient ID#:

Physician: OLLIFFE J

Test: Usher Syndrome Type III

Result:

NEGATIVE
(No mutation identified)

Interpretation:
This individual is negative for the mutation analyzed. For detection rates and a revised carrier risk, see the table below.

Usher Syndrome Type III (USH3, OMIM 276902) is an inherited, autosomal recessive disorder characterized by progressive, postlingual hearing loss and variable severity of retinitis pigmentosa (RP), with or without vestibular phenotype. Unlike most forms of Usher Syndrome, individuals with USH3 are usually born with normal hearing. The progressive hearing loss has been one of the discriminatory features between USH3 and Usher Type I or Usher Type II. Vision loss related to RP generally develops from early childhood to adulthood, although the severity is variable. The clinical finding of vestibular dysfunction is variable as well. The disease has an elevated prevalence in the Ashkenazi Jewish population, with a carrier rate of 1 in 107, although it can be seen in all ethnic groups. When both parents are carriers of USH3, there is a 1 in 4 (25%) chance with each pregnancy to have a child with the disease. Prenatal diagnosis is available.

Molecular genetic testing for USH3 encompasses one mutation in the gene encoding clarin-1 (*USH3A* gene, 3q25.1). Testing for the N48K mutation identifies approximately 98% of USH3 carriers in the Ashkenazi Jewish population. The carrier frequency in the non-Ashkenazi Jewish population has not been determined. A negative result decreases the likelihood that this person is a carrier, but cannot completely eliminate the possibility. The presence of a rare mutation cannot be ruled out. DNA test results must be combined with clinical information for the most accurate interpretation.

This table assumes no family history of Usher Syndrome Type III. Please call (800) 345-4363 for a revised report if this individual has a family history of USH3.

Ethnicity	Detection rate for the *USH3A* mutation	Carrier risk prior to testing (assumes no family history)	Remaining risk given negative result
Ashkenazi Jewish	98%	1/107	1/5301
Other	Not known	Not known	

Mutation:
N48K

Methodology:
DNA analysis of the *USH3A* gene (OMIM 606397) is performed on the Luminex Universal Array Platform using primer extension chemistry. Multiplex PCR amplifies DNA fragments containing the mutation above. Primer extension then generates a biotin-labeled product that hybridizes to complementary, bead-immobilized probes to permit flow-sorted detection of both normal and mutation sequences. Molecular-based testing is highly accurate, but as in any laboratory test, rare diagnostic errors may occur. This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary.

References:

1. Ness SL, Ben-Yosef T, Madeo AC, Brewer CC, Avraham KB, Kornreich R, Desnick RJ, Willner JP, Friedman TB, Grifith AJ. Genetic homogeneity and phenotypic variability among Ashkenazi Jews with Usher Syndrome Type III. J Med Genet, 2003;40:767:772.
2. Ben-Yosef T, Friedman TB. The genetic bases for syndromic and nonsyndromic deafness among Jews. Trends Mol Med.
3. Genetics Home Reference: Usher Syndrome. Located at http://ghr.nlm.nih.gov/condition=ushersyndrome. Accessed on February 24, 2010.

Results Released By: Melissa A. Hayden, Ph.D., Director
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Test Results of: 9896, DONOR
DOB: [redacted] Sex: M
Collected on: 07/02/2015
Received on: 07/02/2015
Reported on: 07/07/2015

Patient ID#:

Branch Number: WAB55
Account Number: 46857540
Specimen Number: 183-129-0716-0
Specimen Type: Blood

Physician: OLLIFFE J

Test: Mucolipidosis Type IV, DNA Analysis

Result:

NEGATIVE
(No mutation identified)

Interpretation:
This individual is negative for the mutations analyzed. For detection rates and a revised carrier risk, see table below.

Mucolipidosis Type IV (MLIV, OMIM 252650), also known as Sialolipidosis is an autosomal recessive neurodegenerative lysosomal storage disorder associated with growth and psychomotor retardation, as well as ophthalmologic abnormalities. The disease has an elevated prevalence among Ashkenazi Jewish individuals, with a carrier rate of approximately 1 in 122. When both parents are carriers of MLIV, there is a 1 in 4 (25%) chance with each pregnancy to have a child with the disease. Prenatal diagnosis is available.

Molecular genetic testing for MLIV encompasses two mutations in the gene encoding mucolipin (*MCOLN1,* 19p13.2). Testing for these mutations identifies 96% of MLIV carriers in the Ashkenazi Jewish population. A negative test result decreases the likelihood that a person is a carrier, but cannot completely eliminate the possibility. The presence of a rare mutation cannot be ruled out. DNA test results must be combined with enzyme test results and clinical information for the most accurate interpretation.

This table assumes no family history of Mucolipidosis Type IV. Please call (800) 345-4363 for a revised report if this individual has a family history of MLIV.

Ethnicity	Detection rate for the *MCOLN1* mutations	Carrier risk prior to testing (assumes no family history)	Remaining risk given negative result
Ashkenazi Jewish	96%	1/122	1/3026
Other	Not known	Not known	

Mutations:
IVS3-2 A>G (486-2 A>G) 511del6434 (del EX1-EX7) C

Methodology:
DNA analysis of the mucolipin (*MCOLN1*) gene (OMIM 605248) is performed on the Luminex Universal Array Platform using primer extension chemistry. Multiplex PCR amplifies DNA fragments containing the mutations above. Primer extension then generates a biotin-labeled product that hybridizes to complementary, bead-immobilized probes to permit flow-sorted detection of both normal and mutation sequences. Molecular-based testing is highly accurate, but as in any laboratory test, rare diagnostic errors may occur. This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary.

References:

1. Bassi, MT, Manzoni, M, Monti, E, Pizzo, MT, Ballabio, A, and Borsani, G. Cloning of the gene encoding a novel integral membrane protein, Mucolipin - and identification of the two major founder mutations causing Mucolipidosis Type IV. Amer. J. Hum. Genet. 2000;67:1110-1120.
2. Edelmann L, et al. Carrier screening for Mucolipidosis Type IV in the American Ashkenazi Jewish population. *Am J Hum Genet.* 2002; 70(4): 1023-1027.
3. Slaugenhaupt, S. The molecular basis of Mucolipidosis Type IV. (2002) *Curr Mol Med* 2:445-450
4. American College of Obstetricians and Gynecologists. Committee Opinion. Washington, DC: ACOG; October 2009, #442.
5. Gross SJ, Pletcher BA, Monaghan KG. Carrier screening in individuals of Ashkenazi Jewish descent. Genet Med 2008; 10(1):54-56.
6. Monaghan KG, Feldman GL, Palomaki GE, Spector EB, et al. Technical standards and guidelines for reproductive screening in the Ashkenazi Jewish population. Genet Med. 2008; 10(1):57-72.

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July 7, 2015

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Test Results of: 9896, DONOR
DOB: [redacted] Sex: M
Collected on: 07/02/2015
Received on: 07/02/2015
Reported on: 07/07/2015

Branch Number: WAB55
Account Number: 46857540
Specimen Number: 183-129-0716-0
Specimen Type: Blood

Patient ID#:

Physician: OLLIFFE J

Test: Walker-Warburg Syndrome

Result:

NEGATIVE **(No mutation identified)**

Interpretation:
This individual is negative for the mutation analyzed. For detection rates and a revised carrier risk, see the table below.

Walker-Warburg Syndrome (WWS, OMIM 253800) is an inherited, autosomal recessive disorder characterized by a triad of brain malformations, eye abnormalities, and congenital muscular dystrophy. The clinical findings include muscle weakness, hypotonia, feeding difficulties, blindness, seizures, and male genital anomalies. Characteristic brain malformations include cobblestone lissenchephaly, among other findings. Life expectancy is less than 3 years. The disease has an elevated prevalence in the Ashkenazi Jewish population, with a carrier rate of 1 in 79. When both parents are carriers of WWS, there is a 1 in 4 (25%) chance with each pregnancy to have a child with the disease. Prenatal diagnosis is available.

Molecular genetic testing for WWS encompasses one founder mutation in the gene encoding fukutin (*FKTN* gene, 9q31). Testing for the c.1167insA mutation identifies greater than 99% of WWS carriers in the Ashkenazi Jewish population. The carrier frequency in the non-Ashkenazi Jewish population has not been determined. A negative result decreases the likelihood that this person is a carrier, but cannot completely eliminate the possibility. The presence of a rare mutation cannot be ruled out. DNA test results must be combined with clinical information for the most accurate interpretation.

This table assumes no family history of Walker-Warburg Syndrome. Please call (800) 345-4363 for a revised report if this individual has a family history of WWS.

Ethnicity	Detection rate for the *FKTN* mutation	Carrier risk prior to testing (assumes no family history)	Remaining risk given negative result
Ashkenazi Jewish	>99%	1/79	1/7801
Other	Not known	Not known	

Mutation:
c.1167insA

Methodology:
DNA analysis of the *FKTN* gene (OMIM 607440) is performed on the Luminex Universal Array Platform using primer extension chemistry. Multiplex PCR amplifies DNA fragments containing the mutation above. Primer extension then generates a biotin-labeled product that hybridizes to complementary, bead-immobilized probes to permit flow-sorted detection of both normal and mutation sequences. Molecular-based testing is highly accurate, but as in any laboratory test, rare diagnostic errors may occur. This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary.

References:

1. Chang W et al. 2009. Founder Futukin mutation causes Walker-Warburg Syndrome in four Ashkenazi Jewish families. *Prenat Diagn.* 29:560-569.
2. Manzini, MC et al. 2008. Ethnically diverse causes of Walker-Warburg Syndrome (WWS): *FCMD* mutations are a more common cause of WWS outside of the Middle East. *Hum Mutat.* 29(11): E231-E241.

Results Released By: Melissa A. Hayden, Ph.D., Director
Report Released By: Melissa Hayden, Ph.D., Director

Arundhati Chatterjee, M.D.
Medical Director

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July 7, 2015

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Test Results of: 9896, DONOR
DOB: [redacted] Sex: M
Collected on: 07/02/2015
Received on: 07/02/2015
Reported on: 07/07/2015

Patient ID#:

Branch Number: WAB55
Account Number: 46857540
Specimen Number: 183-129-0716-0
Specimen Type: Blood

Physician: OLLIFFE J

Test: Niemann-Pick, Type A and B, DNA Analysis

Result:

NEGATIVE **(No mutation identified)**

Interpretation:
This individual is negative for the mutations analyzed. For detection rates and a revised carrier risk, see table below. If Niemann-Pick Disease is a suspected diagnosis for this individual, enzyme analysis is recommended.

Niemann-Pick Disease (Type A, OMIM 257200 and Type B, OMIM 607616) is an autosomal recessive lysosomal storage disorder that is characterized by failure to thrive, and hepatosplenomegaly. This test only analyzes mutations found in Types A and B. Type A is the infantile form that generally leads to death in early childhood. Type B is often called the chronic or non-neuropathic form in which affected individuals have absence of neurologic involvement and prolonged survival. The disease has an elevated prevalence among Ashkenazi Jewish individuals, with a carrier rate of 1 in 90. When both parents are carriers of Niemann-Pick Disease, there is a 1 in 4 (25%) chance with each pregnancy to have a child with the disease. Prenatal diagnosis is available.

Molecular genetic testing for Niemann-Pick Disease, Type A encompasses three mutations in the acid sphingomyelinase gene (*SMPD1*, 11p15.4). Testing for these mutations identifies 95% of Niemann-Pick Disease carriers in the Ashkenazi Jewish population. The ΔR608 mutation is specific for Niemann-Pick Disease, Type B. This test has limited value for people of non-Ashkenazi Jewish ancestry, as the mutation detection rate is negligible. A negative test result decreases the likelihood that a person is a carrier, but cannot completely eliminate the possibility. The presence of a rare mutation cannot be ruled out. DNA test results must be combined with enzyme test results and clinical information for the most accurate interpretation.

This table assumes no family history of Niemann-Pick Disease. Please call (800) 345-4363 for a revised report if this individual has a family history of Niemann-Pick Disease.

Ethnicity	Detection rate for Type A *SMPD1* mutations	Carrier risk prior to testing (assumes no family history)	Remaining risk given negative result
Ashkenazi Jewish	95%	1/90	1/1781
Other	Not known	Not known	

Mutations:
L302P R496L fsP330 ΔR608

Methodology:
DNA analysis of the acid sphingomyelinase (*SMPD1*) gene (OMIM 607608) is performed on the Luminex Universal Array Platform using primer extension chemistry. Multiplex PCR amplifies DNA fragments containing the mutations above. Primer extension then generates a biotin-labeled product that hybridizes to complementary, bead-immobilized probes to permit flow-sorted detection of both normal and mutation sequences. Molecular-based testing is highly accurate, but as in any laboratory test, rare diagnostic errors may occur. This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary.

References:

1. Schuchman EH and Miranda SRP. (1997). Genet Test 1:13-19.
2. American College of Obstetricians and Gynecologists. Committee Opinion. Washington, DC: ACOG; October 2009. #442
3. Gross SJ, Pletcher BA, Monaghan KG. Carrier screening in individuals of Ashkenazi Jewish descent. Genet Med 2008; 10(1):54-56.
4. Monaghan KG, Feldman GL, Palomaki GE, Spector EB, et al. Technical standards and guidelines for reproductive screening in the Ashkenazi Jewish population. Genet Med. 2008; 10(1):57-72.

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Report Released By: Melissa Hayden, Ph.D., Director

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Medical Director

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Patient Report

Specimen ID: 211-129-2581-0
Control ID: B0026086813

Acct #: 46857540 **Phone:** (206) 588-1484 **Rte:** 00

9896, DONOR

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SEATTLE WA 98105

Patient Details
DOB: [redacted]
Age(y/m/d): [redacted]
Gender: M **SSN:**
Patient ID:

Specimen Details
Date collected: 07/29/2015 1510 Local
Date entered: 07/31/2015
Date reported: 08/04/2015 2008 ET

Physician Details
Ordering: J OLLIFFE
Referring:
ID:
NPI: 1306838271

General Comments & Additional Information
Alternate Control Number: B0026086813

Alternate Patient ID: Not Provided

Ordered Items
Tay-Sachs, Biochemical, Serum

TESTS	RESULT	FLAG	UNITS	REFERENCE INTERVAL	LAB
Tay-Sachs, Biochemical, Serum					
% Hex A	59.7		%		01
Total Activity	534.0		nmol/hr/mL		01
Tot Act of Norm Ctrl	933.6		nmol/hr/mL		01

Results:

Result: NON-CARRIER 01

The above biochemical results are consistent with this individual being a non-carrier for Tay-Sachs disease.

Tay-Sachs disease (TSD) is an autosomal recessive lysosomal storage disorder that causes progressive neurological deterioration. TSD is more common in the Ashkenazi Jewish population where approximately 1 in every 25 individuals is a carrier. Both parents must be carriers of TSD in order to have an affected child. When two people who are both carriers for Tay-Sachs disease have children, the couple has a 25% chance with each pregnancy to have an affected child.

% Hex A Reference Intervals:

Non-carrier	>58
Inconclusive	53 - 58
Carrier	34 - 52

Director Review 01

Adviye Ayper Tolun, MS, PhD, FACMG
Director, Biochemical Genetics
To discuss these results or other testing for inborn errors of metabolism, please contact our Biochemical Geneticists at 1-800-345-GENE(4363), LabCorp Genetics Customer Service, RTP, NC.

Methodology 01

Total hexosaminidase (A and B) and hexosaminidase B activities were measured by a modification of the heat inactivation method of Kaback using a synthetic fluorogenic substrate. The activity of hexosaminidase A was calculated as the difference between these activities. Kaback MM (1972) thermal fractionation of serum hexosaminidases: applications to heterozygote detection and diagnosis of Tay-Sachs disease. Methods Enzymol 28:862-867.
LabCorp Genetics Customer Service, RTP, NC:1-800-345-GENE.

Patient: 9896, DONOR
DOB: [redacted]

Control ID: B0026086813

Specimen ID: 211-129-2581-0
Date collected: 07/29/2015 1510 Local

01	TG	LabCorp RTP 1912 TW Alexander Drive, RTP, NC 27709-0150	Arundhati Chatterjee, MD

For inquiries, the physician may contact **Branch: 800-598-3345 Lab: 206-861-7000**

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July 7, 2015

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Test Results of: 9896, DONOR
DOB: [redacted] Sex: M
Collected on: 07/02/2015
Received on: 07/02/2015
Reported on: 07/07/2015

Patient ID#:

Branch Number: WAB55
Account Number: 46857540
Specimen Number: 183-129-0716-0
Specimen Type: Blood

Physician: OLLIFFE J

Test: MSUD, Carrier Testing, DNA

Result:

NEGATIVE
(No mutation identified)

Interpretation:
This individual is negative for the mutations analyzed. For detection rates and a revised carrier risk, see the table below.

Maple Syrup Urine Disease (MSUD, OMIM 248600) is an inherited autosomal recessive disease caused by deficient activity of branched chain alpha-ketoacid dehydrogenase. MSUD can be detected by newborn screening and effectively treated with dietary restriction. Untreated disease is characterized by poor feeding, brain damage, and ultimately coma and death. Even with dietary restriction and monitoring, affected individuals may still have periodic metabolic crises due to infection or stress. Impaired intellectual development or neurological complications can occur as a result of delayed diagnosis. The disease has elevated prevalence among Ashkenazi Jews and Mennonites, with carrier rates of 1 in 81 and 1 in 10, respectively, although it is seen in all ethnic groups. When both parents are carriers of MSUD, there is a 1 in 4 (25%) chance with each pregnancy to have a child with the disease. Prenatal diagnosis is available.

Molecular genetic testing for MSUD encompasses four mutations in two components of the branched-chain ketoacid dehydrogenase complex (BCKAD): the E1α subunit (*BCKDHA*, 19q13.2), and the E1β subunit (*BCKDHB*, 6q14.1), with a detection rate of >99% for both Ashkenazi Jews and Mennonites. Plasma amino acid analysis can be used for diagnostic purposes in affected individuals but cannot determine carrier status. A negative test result decreases the likelihood that a person is a carrier but cannot completely eliminate the possibility. The presence of a rare mutation cannot be ruled out. DNA test results must be combined with clinical information for the most accurate interpretation. *Plasma Amino Acid Profile should be considered if diagnosis or treatment monitoring is desired.*

This table assumes no family history of Maple Syrup Urine Disease. Please call (800) 345-4363 for a revised report if this individual has a family history of MSUD.

Ethnicity	Detection rate for the *BCKDHA* and *BCKDHB* mutations	Carrier risk prior to testing (assumes no family history)	Remaining risk given negative result
Ashkenazi Jewish	>99%	1/81	1/8001
Mennonite*	>99%	1/10	1/901
Other	Not known	Not known	

*-Y438N is the founder mutation for Mennonites.

Mutations:
R183P (E1β subunit) G278S (E1β subunit) E372X (E1β subunit) Y438N (E1α subunit)

Methodology:
DNA analysis of the branched-chain ketoacid dehydrogenase E1, α subunit (*BCKDHA*) gene (OMIM 608348), and β subunit (*BCKDHB*) gene (OMIM 248611) is performed on the Luminex Universal Array Platform using primer extension chemistry. Multiplex PCR amplifies DNA fragments containing the mutations above. Primer extension then generates a biotin-labeled product that hybridizes to complementary, bead-immobilized probes to permit flow-sorted detection of both normal and mutation sequences. Molecular-based testing is highly accurate, but as in any laboratory test, rare diagnostic errors may occur. This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary.

References:

1. Strauss KA, Puffenberger EG, Morton DH. Maple Syrup Urine Disease. www.geneclinics.org [30 January 2006].
2. Edelmann L, Wasserstein MP, Kornreich R, Sansaricq C, Snyderman SE, Diaz GA. Maple Syrup Urine Disease: Identificarion and carrier-frequency determination of a novel founder mutation in the Ashkenazi Jewish population. Am J Hum Genet. 2001;69:863-868.
3. Kornreich R, Edelmann L, Diaz GA, Desnick RJ. High frequency of carriers for Maple Syrup Urine Disease in the Ashkenazi Jewish population [abstract] www.ashg.org/cgi-bin/ashg04. Annual Meeting of the ASHG;2004.

Results Released By: Melissa A. Hayden, Ph.D., Director
Report Released By: Melissa Hayden, Ph.D., Director

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July 7, 2015

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Test Results of: 9896, DONOR
DOB: [redacted] Sex: M
Collected on: 07/02/2015
Received on: 07/02/2015
Reported on: 07/07/2015

Branch Number: WAB55
Account Number: 46857540
Specimen Number: 183-129-0716-0
Specimen Type: Blood

Patient ID#:

Physician: OLLIFFE J

Test: Bloom Syndrome, DNA Analysis

Result:

NEGATIVE
(No mutation identified)

Interpretation:
This individual is negative for the mutation analyzed. For detection rates and a revised carrier risk, see table below. If Bloom Syndrome is a suspected diagnosis for this individual, sister chromatid exchange (SCE) studies are recommended.

Bloom Syndrome (BLM, OMIM 210900) is a rare autosomal recessive disorder that is characterized by small stature, immunodeficiency, chromosomal instability and a predisposition to multiple cancers. The disease has an elevated prevalence among Ashkenazi Jewish individuals, with a carrier rate of 1 in 100. When both parents are carriers of BLM, there is a 1 in 4 (25%) chance with each pregnancy to have a child with the disease. Prenatal diagnosis is available.

Molecular genetic testing for BLM encompasses one mutation in the *RECQ*-like DNA helicase gene (15q26.1). Testing for this mutation identifies greater than 97% of BLM carriers in the Ashkenazi Jewish population. This test has limited value for individuals of non-Ashkenazi Jewish ancestry, as the detection rate is negligible. A negative test result decreases the likelihood that a person is a carrier, but cannot completely eliminate the possibility. The presence of a rare mutation cannot be ruled out. DNA test results must be combined with clinical information for the most accurate interpretation.

This table assumes no family history of Bloom Syndrome. Please call (800) 345-4363 for a revised report if this individual has a family history of Bloom Syndrome.

Ethnicity	Detection rate for the *RECQ*-like DNA helicase mutation	Carrier risk prior to testing (assumes no family history)	Remaining risk given negative result
Ashkenazi Jewish	>97%	1/100	1/3301
Other	Not known		

Mutations:
2281del6ins7

Methodology:
DNA analysis of the *RECQ*-like DNA helicase gene (OMIM 604610) is performed on the Luminex Universal Array Platform using primer extension chemistry. Multiplex PCR amplifies DNA fragments containing the mutation 2281del6ins7. Primer extension then generates a biotin-labeled product that hybridizes to complementary, bead-immobilized probes to permit flow-sorted detection of both normal and mutation sequences. Molecular-based testing is highly accurate, but as in any laboratory test, rare diagnostic errors may occur. This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary.

References:

1. Shahrabani L *et al.* (1998). Genet Test 2:293-296.
2. American College of Obstetricians and Gynecologists. Committee Opinion. Washington, DC: ACOG; October 2009. #442
3. Gross SJ, Pletcher BA, Monaghan KG. Carrier screening in individuals of Ashkenazi Jewish descent. Genet Med 2008; 10(1):54-56.
4. Monaghan KG, Feldman GL, Palomaki GE, Spector EB, et al. Technical standards and guidelines for reproductive screening in the Ashkenazi Jewish population. Genet Med. 2008; 10(1):57-72.

Results Released By: Melissa A. Hayden, Ph.D., Director
Report Released By: Melissa Hayden, Ph.D., Director

Arundhati Chatterjee, M.D.
Medical Director

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Test Results of: 9896, DONOR
DOB: [redacted] Sex: M
Collected on: 07/02/2015
Received on: 07/02/2015
Reported on: 07/07/2015

Branch Number: WAB55
Account Number: 46857540
Specimen Number: 183-129-0716-0
Specimen Type: Blood

Patient ID#:

Physician: OLLIFFE J

Test: Nemaline Myopathy

Result:

NEGATIVE
(No mutation identified)

Interpretation:
This individual is negative for the mutation analyzed. For detection rates and a revised carrier risk, see the table below.

Nemaline Myopathy (NM, OMIM 256030) is an inherited, autosomal recessive disorder characterized by weakness, hypotonia and depressed or absent deep tendon reflexes. Muscle weakness is usually most severe in the face, the neck flexors and the proximal limb muscles. NM shows a wide range of clinical variability. The disease has an elevated prevalence in the Ashkenazi Jewish population, with a carrier rate of 1 in 149. When both parents are carriers of NM, there is a 1 in 4 (25%) chance with each pregnancy to have a child with the disease. Prenatal diagnosis is available.

Molecular genetic testing for NM encompasses one mutation in the gene encoding nebulin (*NEB* gene, 2q23.3). Testing for this mutation identifies greater than 99% of NM carriers in the Ashkenazi Jewish population. The carrier frequency in the non-Ashkenazi Jewish population has not been determined. A negative result decreases the likelihood that this person is a carrier, but cannot completely eliminate the possibility. The presence of a rare mutation cannot be ruled out. DNA test results must be combined with clinical information for the most accurate interpretation.

This table assumes no family history of Nemaline Myopathy. Please call (800) 345-4363 for a revised report if this individual has a family history of NM.

Ethnicity	Detection rate for the *NEB* mutation	Carrier risk prior to testing (assumes no family history)	Remaining risk given negative result
Ashkenazi Jewish	>99%	1/149	1/14801
Other	Not known	Not known	

Mutation:
R2478_D2512del

Methodology:
DNA analysis of the *NEB* gene (OMIM 161650) is performed on the Luminex Universal Array Platform using primer extension chemistry. Multiplex PCR amplifies DNA fragments containing the mutation above. Primer extension then generates a biotin-labeled product that hybridizes to complementary, bead-immobilized probes to permit flow-sorted detection of both normal and mutation sequences. Molecular-based testing is highly accurate, but as in any laboratory test, rare diagnostic errors may occur. This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary.

References:
1. Anderson S, et al. Hum Genet. 2004; 115:185-190.

Results Released By: Melissa A. Hayden, Ph.D., Director
Report Released By: Melissa Hayden, Ph.D., Director

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Test Results of: 9896, DONOR
DOB: [redacted] Sex: M
Collected on: 07/02/2015
Received on: 07/02/2015
Reported on: 07/07/2015

Patient ID#:

Branch Number: WAB55
Account Number: 46857540
Specimen Number: 183-129-0716-0
Specimen Type: Blood

Physician: OLLIFFE J

Test: Usher Syndrome Type IF

Result:

NEGATIVE
(No mutation identified)

Interpretation:
This individual is negative for the mutation analyzed. For detection rates and a revised carrier risk, see the table below.

Usher Syndrome is an autosomal recessive disorder characterized by bilateral sensorineural hearing loss and progressive loss of vision due to retinitis pigmentosa. There are three clinical subtypes of Usher Syndrome, and Type I (USH1 OMIM 276900) is the most severe. Individuals with Type I have profound prelingual hearing loss, vestibular areflexia, and prepubertal onset of retinitis pigmentosa. Seven loci have been mapped for Usher Syndrome, Type I (USH1A-USH1G) and five genes that cause this disorder have been identified. The disease has an elevated prevalence in the Ashkenazi Jewish population, with a carrier rate of 1 in 141. When both parents are carriers of USH1F, there is a 1 in 4 (25%) chance with each pregnancy to have a child with the disease. Prenatal diagnosis is available.

Molecular genetic testing for USH1F encompasses one mutation in the *PCDH15* gene (10q21.1). Testing for the R245X mutation identifies approximately 75% of USH1F carriers in the Ashkenazi Jewish population. The carrier frequency in the non-Ashkenazi Jewish population has not been determined. A negative result decreases the likelihood that this person is a carrier, but cannot completely eliminate the possibility. The presence of a rare mutation cannot be ruled out. DNA test results must be combined with clinical information for the most accurate interpretation.

This table assumes no family history of Usher Syndrome Type 1F. Please call (800) 345-4363 for a revised report if this individual has a family history of USH1F.

Ethnicity	Detection rate for the *PCDH15* mutation	Carrier risk prior to testing (assumes no family history)	Remaining risk given negative result
Ashkenazi Jewish	75%	1/141	1/561
Other	Not known	Not known	

Mutation:
R245X

Methodology:
DNA analysis of the *PCDH15* gene (OMIM 605514) is performed on the Luminex Universal Array Platform using primer extension chemistry. Multiplex PCR amplifies DNA fragments containing the mutation above. Primer extension then generates a biotin-labeled product that hybridizes to complementary, bead-immobilized probes to permit flow-sorted detection of both normal and mutation sequences. Molecular-based testing is highly accurate, but as in any laboratory test, rare diagnostic errors may occur. This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary.

References:

1. Keats BJB, Letz J. Usher Syndrome Type 1. www.geneclinics.org, [28 May 2009].
2. Ben-Yosef T, Ness SL, Madeo AC, Bar-Lev A, Wolfman JH, Ahmed ZM, Desnick RJ, Willner JP, Avraham KB, Ostrer H, Oddoux C, Griffith AJ, Friedman TB. A mutation of *PCDH15* among Ashkenazi Jews with Type 1 Usher Syndrome. N Engl J Med. 2003;348:1664-1670.
3. Browstein Z, Ben Yosef T, Dagan O, Frydman M, Abeliovich D, Sagi M, Abraham FA, Taitelbaum-Swead R, Shohat M, Hildesheimer M, Friedman TB, Avraham KB. The R245X mutation of *PCDH15* in Ashkenazi Jewish children diagnosed with nonsyndromic hearing loss foreshadows retinitis pigmentosa. Pediatr Res 2004;55:995-1000.

Results Released By: Melissa A. Hayden, Ph.D., Director
Report Released By: Melissa Hayden, Ph.D., Director

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July 7, 2015

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Test Results of: 9896, DONOR
DOB: [redacted] Sex: M
Collected on: 07/02/2015
Received on: 07/02/2015
Reported on: 07/07/2015

Patient ID#:

Branch Number: WAB55
Account Number: 46857540
Specimen Number: 183-129-0716-0
Specimen Type: Blood

Physician: OLLIFFE J

Test: Canavan Disease, DNA Analysis

Result:

NEGATIVE
(No mutation identified)

Interpretation:
This individual is negative for the mutations analyzed. For detection rates and a revised carrier risk, see table below.

Canavan Disease (OMIM 217900) is an autosomal recessive progressive leukodystrophy that often leads to death in the first decade of life. It is caused by a deficiency of the enzyme, aspartoacylase (ASPA). Canavan Disease has an elevated prevalence in the Ashkenazi Jewish population, with a carrier rate of approximately 1 in 57. When both parents are carriers of Canavan Disease, there is a 1 in 4 (25%) chance with each pregnancy to have a child with the disease. Prenatal diagnosis is available.

Molecular genetic testing for Canavan Disease encompasses four mutations in the *ASPA* gene (17p13.2). Testing for these mutations identifies approximately 98% of the Canavan Disease carriers in the Ashkenazi Jewish population, and approximately 60% in the non-Jewish Caucasian population. The A305E mutation is typically found among individuals of non-Ashkenazi Jewish ancestry. A negative result decreases the likelihood that this person is a carrier, but cannot completely eliminate the possibility. The presence of a rare mutation cannot be ruled out. DNA test results must be combined with clinical information for the most accurate interpretation.

This table assumes no family history of Canavan Disease. Please call (800) 345-4363 for a revised report if this individual has a family history of Canavan Disease.

Ethnicity	Detection rate for the *ASPA* mutations	Carrier risk prior to testing (assumes no family history)	Remaining risk given negative test result
Ashkenazi Jewish	98%	1/57	1/2801
non-Jewish, Caucasian	~60%	Not known	
Other	Not known	Not known	

Mutations:

E285A (A854C)	Y231X (C693A)	A305E (C914A)	433-2 A>G

Methodology:
DNA analysis of the aspartoacylase *(ASPA)* gene (OMIM 608034) is performed on the Luminex Universal Array Platform using primer extension chemistry. Multiplex PCR amplifies DNA fragments containing the mutations above. Primer extension then generates a biotin-labeled product that hybridizes to complementary, bead-immobilized probes to permit flow-sorted detection of both normal and mutation sequences. Molecular-based testing is highly accurate, but as in any laboratory test, rare diagnostic errors may occur. This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary.

References:

1. Matalon R. (1998). Genet Test 1:21-25.
2. Feigenbaum A, et al. Canavan Disease: carrier frequency determination in the Ashkenazi Jewish population and development of a novel molecular diagnostic assay. Am J Med Genet. 2004; 124A(2):142-147.
3. American College of Obstetricians and Gynecologists. Committee Opinion. Washington, DC; 2009. #442
4. Gross SJ, Pletcher BA, Monaghan KG. Carrier screening in individuals of Ashkenazi Jewish descent. Genet Med 2008; 10(1):54-56.
5. Monaghan KG, Feldman GL, Palomaki GE, Spector EB, et al. Technical standards and guidelines for reproductive screening in the Ashkenazi Jewish population. Genet Med. 2008; 10(1):57-72.

Results Released By: Melissa A. Hayden, Ph.D., Director
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Arundhati Chatterjee, M.D.
Medical Director

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July 7, 2015

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Test Results of: 9896, DONOR
DOB: [redacted] Sex: M
Collected on: 07/02/2015
Received on: 07/02/2015
Reported on: 07/07/2015

Branch Number: WAB55
Account Number: 46857540
Specimen Number: 183-129-0716-0
Specimen Type: Blood

Patient ID#:

Physician: OLLIFFE J

Test: Familial Dysautonomia, DNA Analysis

Result:

NEGATIVE
(No mutation identified)

Interpretation:
This individual is negative for the mutations analyzed. For detection rates and a revised carrier risk, see table below.

Familial Dysautonomia (OMIM 223900), also known as Riley-Day syndrome, is an autosomal recessive disorder that is characterized by absence of papillae of the tongue, diminished tear flow, erythematous blotching of the skin, difficulties with swallowing, relative insensitivity to pain and reduced life expectancy. The disease has an elevated prevalence in the Ashkenazi Jewish population, with a carrier rate of 1 in 30. When both parents are carriers of Familial Dysautonomia, there is a 1 in 4 (25%) chance with each pregnancy to have a child with the disease. Prenatal diagnosis is available.

Molecular genetic testing for Familial Dysautonomia encompasses two mutations in the *IKBKAP* gene (9q31.3). Testing for these two mutations identifies approximately greater than 99.5% of the Familial Dysautonomia carriers in the Ashkenazi Jewish population. The carrier frequency in the non-Ashkenazi Jewish population has not been determined. A negative test result decreases the likelihood that a person is a carrier, but cannot completely eliminate the possibility. The presence of a rare mutation cannot be ruled out. DNA test results must be combined with clinical information for the most accurate interpretation.

This table assumes no family history of Familial Dysautonomia. Please call (800) 345-4363 for a revised report if this patient has a family history of Familial Dysautonomia.

Ethnicity	Detection rate for the *IKBKAP* mutations	Carrier risk prior to testing (assumes no family history)	Remaining risk given negative result
Ashkenazi Jewish	>99.5%	1/30	1/5801
Other	Not known		

Mutations:
IVS20+6T>C R696P

Methodology:
DNA analysis of the Inhibitor of Kappa Light Polypeptide Gene Enhancer (*IKBKAP*) gene (OMIM 603722) is performed on the Luminex Universal Array Platform using primer extension chemistry. Multiplex PCR amplifies DNA fragments containing the mutations, IVS20+6T>C and R696P. Primer extension then generates a biotin-labeled product that hybridizes to complementary, bead-immobilized probes to permit flow-sorted detection of both normal and mutation sequences. Molecular-based testing is highly accurate, but as in any laboratory test, rare diagnostic errors may occur. This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary.

References:

1. Anderson SL *et al.* (2001). Am J Hum Genet 68:753-758.
2. Slaugenhaupt SA *et al.* (2001). Am J Hum Genet 68:598-605.
3. American College of Obstetricians and Gynecologists. Committee Opinion. Washington, DC; 2009. #442
4. Gross SJ, Pletcher BA, Monaghan KG. Carrier screening in individuals of Ashkenazi Jewish descent. Genet Med 2008; 10(1):54-56.
5. Monaghan KG, Feldman GL, Palomaki GE, Spector EB, et al. Technical standards and guidelines for reproductive screening in the Ashkenazi Jewish population. Genet Med. 2008; 10(1):57-72.

Results Released By: Melissa A. Hayden, Ph.D., Director
Report Released By: Melissa Hayden, Ph.D., Director

Arundhati Chatterjee, M.D.
Medical Director

LabCorp
1912 Alexander Drive, RTP, NC, 27709 (800) 345-4363

LabCorp
Laboratory Corporation of America

July 7, 2015

Seattle Sperm Bank
4915 25th Ave Ne Ste 204
SEATTLE, WA 98105

Test Results of: 9896, DONOR
DOB: [redacted] Sex: M
Collected on: 07/02/2015
Received on: 07/02/2015
Reported on: 07/07/2015

Patient ID#:

Branch Number: WAB55
Account Number: 46857540
Specimen Number: 183-129-0716-0
Specimen Type: Blood

Physician: OLLIFFE J

Test: Dihydrolipoamide Dehydrogenase

Result:

NEGATIVE
(No mutation identified)

Interpretation:
This individual is negative for the mutations analyzed. For detection rates and a revised carrier risk, see the table below.

Dihydrolipoamide Dehydrogenase Deficiency (DLD, OMIM 248600) is an inherited, autosomal recessive disorder. It is also known as Maple Syrup Urine Disease Type 3 due to the characteristic maple syrup smell of the urine. DLD is characterized by severe lactic acidosis between 8 weeks and 6 months of age, followed by progressive neurological degeneration with hypotonia, developmental delay, and movement problems. Along with lactic acidosis, additional biochemical findings can include moderate elevation of branch chain amino acids, hyperalaninemia, and elevated liver transaminases. The disease has an elevated prevalence in the Ashkenazi Jewish population, with a carrier rate of 1 in 96. When both parents are carriers of DLD, there is a 1 in 4 (25%) chance with each pregnancy to have a child with the disease. Prenatal diagnosis is available.

Molecular genetic testing encompasses two mutations in the DLD gene (7q31-q32). Testing for the G229C and 105insA (Y35X) mutations identifies approximately 95% of DLD carriers in the Ashkenazi Jewish population. The carrier frequency in the non-Ashkenazi Jewish population has not been determined. A negative result decreases the likelihood that this person is a carrier, but cannot completely eliminate the possibility. The presence of a rare mutation cannot be ruled out. DNA test results must be combined with clinical information for the most accurate interpretation. Plasma amino acid analysis can be used for diagnostic purposes in affected individuals but cannot determine carrier status. *Plasma Amino Acid Profile should be considered if diagnosis or treatment monitoring is desired.*

This table assumes no family history of Dihydrolipoamide Dehydrogenase Deficiency. Please call (800) 345-4363 for a revised report if this individual has a family history of DLD.

Ethnicity	Detection rate for the DLD mutations	Carrier risk prior to testing (assumes no family history)	Remaining risk given negative result
Ashkenazi Jewish	95%	1/96	1/1901
Other	Not known	Not known	

Mutations:
G229C 105insA (Y35X)

Methodology:
DNA analysis of the *DLD* gene (OMIM 238331) is performed on the Luminex Universal Array Platform using primer extension chemistry. Multiplex PCR amplifies DNA fragments containing the mutations above. Primer extension then generates a biotin-labeled product that hybridizes to complementary, bead-immobilized probes to permit flow-sorted detection of both normal and mutation sequences. Molecular-based testing is highly accurate, but as in any laboratory test, rare diagnostic errors may occur. This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary.

References:

1. Shaag A, et al. Am J Med Genet. 1999; 82:177-182.
2. Hong YS, et al. J Inherit Metab Dis. 2003; 26:816-818.
3. Cameron JM, et al. Am J Med Genet. 2006; 140A: 1542-1552.
4. Sansaricq S, et al. J Inherit Metab Dis. 2005; 29:203-204.

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Report Released By: Melissa Hayden, Ph.D., Director

Arundhati Chatterjee, M.D.
Medical Director

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July 7, 2015

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Test Results of: 9896, DONOR
DOB: [redacted] Sex: M
Collected on: 07/02/2015
Received on: 07/02/2015
Reported on: 07/07/2015

Branch Number: WAB55
Account Number: 46857540
Specimen Number: 183-129-0716-0
Specimen Type: Blood

Patient ID#:

Physician: OLLIFFE J

Test: Fanconi Anemia, Type C, DNA Analysis

Result:

NEGATIVE
(No mutation identified)

Interpretation:
This individual is negative for the mutations analyzed. For detection rates and a revised carrier risk, see table below. If Fanconi Anemia is a suspected diagnosis for this individual, chromosome instability studies are recommended.

Fanconi Anemia group C (FAC, OMIM 227645) is a rare autosomal recessive disorder with a highly variable clinical presentation. Patients have bone marrow failure (aplastic anemia) and may develop other blood disorders, such as pancytopenia, myelodysplasia, or acute myelogenous leukemia. Other anomalies can also occur, which may include short stature, café-au-lait spots, arm and thumb anomalies, and renal malformations. The disease has an elevated prevalence in the Ashkenazi Jewish population, with a carrier rate of 1 in 89. When both parents are carriers of FAC, there is a 1 in 4 (25%) chance with each pregnancy to have a child with the disease. Prenatal diagnosis is available.

Molecular genetic testing for FAC encompasses two mutations in the *FANCC* gene (9q22.32). Testing for the IVS4+4 A>T and 322delG mutations identifies approximately 99% of FAC carriers in the Ashkenazi Jewish population. A negative test result decreases the likelihood that a person is a carrier, but cannot completely eliminate the possibility. The presence of a rare mutation cannot be ruled out. DNA test results must be combined with clinical information for the most accurate interpretation.

This table assumes no family history of Fanconi Anemia group C. Please call (800) 345-4363 for a revised report if this individual has a family history of FAC.

Ethnicity	Detection rate for the *FANCC* mutations	Carrier risk prior to testing (assumes no family history)	Remaining risk given negative result
Ashkenazi Jewish	99%	1/89	1/8801
Other	Not known	Not known	

Mutations:
IVS4+4 A>T 322delG

Methodology:
DNA analysis of the Fanconi Anemia group C *(FANCC)* gene (OMIM 613899) is performed on the Luminex Universal Array Platform using primer extension chemistry. Multiplex PCR amplifies DNA fragments containing the mutations above. Primer extension then generates a biotin-labeled product that hybridizes to complementary, bead-immobilized probes to permit flow-sorted detection of both normal and mutation sequences. Molecular-based testing is highly accurate, but as in any laboratory test, rare diagnostic errors may occur. This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary.

References:

1. Auerbach A. (1997). Genet Test 1:27-32.
2. Verlander PC, Kaporis A, Liu Q, et al. Blood (1995) 86:4034-4038.
3. Yamashita T, Wu, N, Kupfer G, et al. Blood (1996) 87:4424-4432.
4. American College of Obstetricians and Gynecologists. Committee Opinion. Washington, DC; 2009. #442
5. Gross SJ, Pletcher BA, Monaghan KG. Carrier screening in individuals of Ashkenazi Jewish descent. Genet Med 2008; 10(1):54-56.
6. Monaghan KG, Feldman GL, Palomaki GE, Spector EB, et al. Technical standards and guidelines for reproductive screening in the Ashkenazi Jewish population. Genet Med. 2008; 10(1):57-72.

Results Released By: Melissa A. Hayden, Ph.D., Director
Report Released By: Melissa Hayden, Ph.D., Director

Arundhati Chatterjee, M.D.
Medical Director

LabCorp
1912 Alexander Drive, RTP, NC, 27709 (800) 345-4363

LabCorp
Laboratory Corporation of America

Patient Report

Specimen ID: 183-129-0716-0
Control ID: B0024828062

Acct #: 46857540 **Phone:** (206) 588-1484 **Rte:** 00

9896, DONOR

Seattle Sperm Bank
4915 25th Ave Ne Ste 204
SEATTLE WA 98105

Patient Details
DOB: [redacted]
Age(y/m/d): [redacted]
Gender: M **SSN:**
Patient ID:

Specimen Details
Date collected: 07/02/2015 1120 Local
Date entered: 07/02/2015
Date reported: 07/14/2015 0919 ET

Physician Details
Ordering: J OLLIFFE
Referring:
ID:
NPI: 1306838271

General Comments & Additional Information
Alternate Control Number: B0024828062 **Alternate Patient ID:** Not Provided

Ordered Items
Ashkenazi Jew Carrier Complete

TESTS	RESULT	FLAG	UNITS	REFERENCE INTERVAL	LAB
Ashkenazi Jew Carrier Complete					
CF, Screen					01
Molecular analysis report has been mailed.					
Comment:					01
The assay provides information intended to be used for carrier screening in adults of reproductive age, as an aid in newborn screening, and as a confirmatory test for another medically established diagnosis in newborns and children. The test is not indicated for use in fetal diagnostic testing, pre-implantation screening, or for any stand-alone diagnostic purposes without confirmation by another medically established diagnostic product or procedure.					
Gaucher Disease, DNA					01
Molecular analysis report has been mailed.					
Canavan Disease, DNA					01
Molecular analysis report has been mailed.					
Fanconi Anemia C					01
Molecular analysis report has been mailed.					
Glycogen Storage Disease 1a					01
Molecular analysis report has been mailed.					
Maple Syrup Urine Disease					01
Molecular analysis report has been mailed.					
Niemann-Pick Disease					01
Molecular analysis report has been mailed.					
Familial Dysautonomia					01
Molecular analysis report has been mailed.					
Mucolipidosis Type IV Mutation					01
Molecular analysis report has been mailed.					
Bloom Syndrome, DNA Analysis					01
Molecular analysis report has been mailed.					
Tay-Sachs Disease Leukocytes					01
% Hex A	45.7		%		01
Total Activity	1258.6		nmol/hr/mg prot		01
Tot Act of Norm Ctrl	1428.5		nmol/hr/mg prot		01
Interpretation	Result: Carrier				01

Date Issued: 07/15/15 1109 ET

FINAL REPORT

Patient: 9896, DONOR
DOB: [redacted]

Control ID: B0024828062

Specimen ID: 183-129-0716-0
Date collected: 07/02/2015 1120 Local

TESTS	RESULT	FLAG	UNITS	REFERENCE INTERVAL	LAB

The above biochemical results are consistent with this individual being a carrier for Tay-Sachs disease. Should this individual have children with a partner who is also a carrier for Tay-Sachs disease, the couple would have a 25% chance with each pregnancy to have an affected child. Confirmation of this individual's carrier status by Tay-Sachs DNA mutation analysis, screening of this individual's partner and genetic counseling is recommended.
Note that approxmately 38% of non-Jewish and 3% of Jewish individuals who are identified as carriers for Tay-Sachs disease by enzyme analysis actually have a pseudodeficiency mutation in the Tay-Sachs gene. These individuals are NOT at increased risk to have a child affected with Tay-Sachs disease. Confirmation of carrier status by DNA testing is recommended to rule out the presence of a pseudodeficiency mutation.

% Hex A Ranges:

Non-carrier	>59%
Inconclusive	53 - 59%
Carrier	35 - 52%

Director Review
Suzette M. Huguenin, PhD, FACMG
Director, Biochemical and Molecular Genetics
To discuss these results or other testing for inborn errors of metabolism, please contact our Biochemical Geneticists at 1-800-345-GENE(4363), LabCorp Genetics Customer Service, RTP, NC. 01

Methodology 01
Total hexosaminidase (A and B) and hexosaminidase B activities were measured by a modification of the heat inactivation method of Kaback using a synthetic fluorogenic substrate. The activity of hexosaminidase A was calculated as the difference between these activities. Kaback MM (1972) thermal fractionation of serum hexosaminidases: applications to heterozygote detection and diagnosis of Tay-Sachs disease. Methods Enzymol 28:862-867.
LabCorp Genetics Customer Service, RTP, NC:1-800-345-GENE.

Nemaline Myopathy 01
Molecular analysis report has been mailed.

Usher Syndrome Type III 01
Molecular analysis report has been mailed.

Usher Syndrome Type IF 01
Molecular analysis report has been mailed.

Familial Hyperinsulinism 01
Molecular analysis report has been mailed.

Dihydrolipoamide Dehydrogenase 01
Molecular analysis report has been mailed.

Walker-Warburg Syndrome 01
Molecular analysis report has been mailed.

Joubert Syndrome Type II 01
Molecular analysis report has been mailed.

01	TG	LabCorp RTP 1912 TW Alexander Drive, RTP, NC 27709-0150	Arundhati Chatterjee, MD

For inquiries, the physician may contact **Branch: 800-598-3345 Lab: 206-861-7000**

July 7, 2015

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Test Results of: 9896, DONOR
DOB: [redacted] Sex: M
Collected on: 07/02/2015
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Branch Number: WAB55
Account Number: 46857540
Specimen Number: 183-129-0716-0
Specimen Type: Blood

Patient ID#:

Physician: OLLIFFE J

Test: Familial Hyperinsulinism

Result:

NEGATIVE
(No mutation identified)

Interpretation:
This individual is negative for the mutations analyzed. For detection rates and a revised carrier risk, see the table below.

Familial Hyperinsulinism (FHI, OMIM 256450) is a rare disorder caused by overproduction of insulin in the pancreas, most commonly inherited in a recessive manner. Overproduction of insulin results in severe hypoglycemia (low blood sugar). Newborns with FHI caused by mutations in the *ABCC8* gene are typically large for gestational age and present with severe refractory bypoglycemia within 48 hours of life. These individuals often only have a partial therapeutic response to diet and medical management and many require pancreatic resection. If left untreated, FHI may cause irreversible neurological damage and is potentially lethal. This disease has an elevated prevalence in the Ashkenazi Jewish population, with a carrier rate of 1 in 66. When both parents are carriers of FHI, there is a 1 in 4 (25%) chance with each pregnancy to have a child with the disease. Prenatal diagnosis is available.

There are several genes known to be associated with FHI. Molecular genetic testing for two *ABCC8* gene (11p15.1) founder mutations identifies approximately 88% of FHI carriers in the Ashkenazi Jewish population. The carrier frequency in the non-Ashkenazi Jewish population has not been determined. A negative result decreases the likelihood that this person is a carrier, but cannot completely eliminate the possibility. The presence of a rare mutation cannot be ruled out. DNA test results must be combined with clinical information for the most accurate interpretation.

This table assumes no family history of Familial Hyperinsulinism. Please call (800) 345-4363 for a revised report if this individual has a family history of FHI.

Ethnicity	Detection rate for the *ABCC8* mutations	Carrier risk prior to testing (assumes no family history)	Remaining risk given negative result
Ashkenazi Jewish	88%	1/66	1/542
Other	Not known		

Mutations:
F1388del 3992-9G-to-A

Methodology:
DNA analysis of the *ABCC8* gene (OMIM 600509) is performed on the Luminex Universal Array Platform using primer extension chemistry. Multiplex PCR amplifies DNA fragments containing the mutations above. Primer extension then generates a biotin-labeled product that hybridizes to complementary, bead-immobilized probes to permit flow-sorted detection of both normal and mutation sequences. Molecular-based testing is highly accurate, but as in any laboratory test, rare diagnostic errors may occur. This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary.

References:
1. Nestorowicz A, et al. Hum Mol Genet. 1996; 5(11): 1813-1822.

Results Released By: Melissa A. Hayden, Ph.D., Director
Report Released By: Melissa Hayden, Ph.D., Director

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July 7, 2015

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Test Results of: 9896, DONOR
DOB: [redacted] Sex: M
Collected on: 07/02/2015
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Reported on: 07/07/2015

Branch Number: WAB55
Account Number: 46857540
Specimen Number: 183-129-0716-0
Specimen Type: Blood

Patient ID#:

Physician: OLLIFFE J

Test: GLYCOGEN STORAGE DISEASE 1A

Result:

NEGATIVE
(No mutation identified)

Interpretation:
This individual is negative for the mutations analyzed. For detection rates and a revised carrier risk, see the table below.

Glycogen Storage Disease Type 1a (GSD1a), also called Von Gierke Disease (OMIM 232200), is an inherited autosomal recessive disorder characterized by an enlarged liver and kidneys due to the accumulation of glycogen and fat. Some infants that are untreated develop severe hypoglycemia (low blood sugar). Long-term complications of untreated GSD1a include short stature, osteoporosis, delayed puberty, kidney disease, liver disease, seizures, and mental retardation. This condition is caused by a deficiency of the enzyme D-glucose-6-phosphatase (G6Pase), and can be treated by making dietary changes and maintaining normal levels of glucose to prevent hypoglycemia. Individuals who are treated can be expected to have normal growth and many live into adulthood. The disease has elevated prevalence among Ashkenazi Jews, with a carrier rate of 1 in 71, although it is seen in all ethnic groups. When both parents are carriers of GSD1a, there is a 1 in 4 (25%) chance with each pregnancy to have a child with the disease. Prenatal diagnosis is available.

Molecular genetic testing for GSD1a encompasses two mutations in the gene encoding D-glucose-6-phosphatase (17q21.31). Testing for these two mutations identifies 99% of GSD1a carriers that are Ashkenazi Jewish and approximately 60% of GSD1a carriers that are non-Ashkenazi Jewish Caucasian. Biochemical analysis of liver biopsy specimens can be performed for diagnostic purposes but does not determine carrier status. A negative test result decreases the likelihood that a person is a carrier, but cannot completely eliminate the possibility. The presence of a rare mutation cannot be ruled out. DNA test results must be combined with clinical information for the most accurate interpretation.

This table assumes no family history of Glycogen Storage Disease 1a. Please call (800) 345-4363 for a revised report if this individual has a family history of GSD1a.

Ethnicity	Detection rate for the *G6Pase* mutations	Carrier risk prior to testing (assumes no family history)	Remaining risk given negative result
Ashkenazi Jewish	>99%	1/71	1/7001
non-Ashkenazi Jewish, Caucasian	~60%	1/158	1/393

Mutations:
R83C Q347X

Methodology:
DNA analysis of the D-glucose-6-photophatase gene (*G6Pase*, OMIM 611045) is performed on the Luminex Universal Array Platform using primer extension chemistry. Multiplex PCR amplifies DNA fragments containing the mutations above. Primer extension then generates a biotin-labeled product that hybridizes to complementary, bead-immobilized probes to permit flow-sorted detection of both normal and mutation sequences. Molecular-based testing is highly accurate, but as in any laboratory test, rare diagnostic errors may occur. This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary.

References:

1. Bali DS, Chen YT. Glycogen Storage Disease Type 1. www.geneclinics.org, [19 April 2006].
2. Ekstein J, Rubin BY, Anderson SL, Weinstein DA, Bach G, Abeliovich D, Webb M, Risch N. Mutation frequencies for Glycogen Storage Disease Ia in the Ashkenazi Jewish population. Am J Hum genet. 2004;129A:162-164.
3. Chou JY, Matern D, Mansfield BC, Chen YT. Type I Glycogen Storage Diseases: disorders of the glucose-6-phosphatase complex. Curr Mol Med. 2002;2:121-143.
4. Lei KJ, Chen YT, Ken H, Wong LJ, Liu JL, McConkie-Rosell A, Van Hove JL, Ou HC, Yeh NJ, Pan LY. Genetic basis of Glycogen Storage Disease Type 1a: prevalent mutations at the glucose-6-phosphatase locus. Am J Hum Genet. 1995;57:766-771.

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