Donor 6739-PRS

Genetic Testing Summary

Fairfax Cryobank recommends reviewing this genetic testing summary with your healthcare provider to determine suitability.

Last Updated: 08/27/18

Donor Reported Ancestry: Polish, Portuguese, Filipino, Spanish Jewish Ancestry: No

Genetic Test*	Result	Comments/Donor's Residual Risk**
Chromosome analysis (karyotype)	Normal male karyotype	No evidence of clinically significant chromosome abnormalities
Hemoglobin evaluation	Normal hemoglobin fractionation and MCV/MCH results	Reduced risk to be a carrier for sickle cell anemia, beta thalassemia, alpha thalassemia trait (aa/-- and a-/a-) and other hemoglobinopathies
Cystic Fibrosis (CF) carrier screening	Negative by genotyping of 97 mutations- in the CFTR gene	1/343
Spinal Muscular Atrophy (SMA) carrier screening	Negative for deletions of exon 7 in the SMN1 gene	1/632

*No single test can screen for all genetic disorders. A negative screening result significantly reduces, but cannot eliminate, the risk for these conditions in a pregnancy.

**Donor residual risk is the chance the donor is still a carrier after testing negative.

LabCorp
Laboratory Corporation of America

September 16, 2010

[redacted]

Test Results of: DONOR, 6739
DOB: 09/22/1982 Age: 27.9 Y Sex: M
Collected on: 09/09/2010
Received on: 09/09/2010
Reported on: 09/16/2010

Patient ID#:

Branch Number: CAB60
Account Number: 04316522
Specimen Number: 252-086-0889-0
Specimen Type: Blood

genzyme

Cystic Fibrosis Mutation Analysis

Patient Name: Donor# 6739, .
Referring Physician: Madelyn Kahn, MD
Specimen #: 17195492
Patient ID: 17127871-17

Client #: 880107
Case #: 17337940

DOB: [redacted]
Sex: M
SSN:

Date Collected: 09/09/2010
Date Received: 09/10/2010
Lab ID:
Hospital ID:
Specimen Type: **BLDPER**

Pacific Reproductive Services
444 De Haro Street
Suite 222
San Francisco CA 94107

RESULTS REVIEWED BY:

DISCUSSED WITH:
RECIPIENT DONOR NA
OK TO FILE Y N
DATE: 9/16/10

Ethnicity: Asian, Caucasian, Hispanic

Indication: Carrier test / Gamete donor

RESULTS: Negative for the 97 mutations analyzed

INTERPRETATION

This individual is negative for the mutations analyzed. This result reduces but does not eliminate the risk to be a CF carrier.

COMMENTS:

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	References
African American	1/65 to 1/338	81%	Genet in Med 3:168, 2001
Ashkenazi Jewish	1/26 to 1/834	97%	Am J Hum Genet 51:951, 1994
Asian		Not Provided	Insufficient data
Caucasian	1/25 to 1/343	93%	Genet in Med 3:168, 2001; Genet in Med 4:90, 2002
Hispanic	1/46 to 1/205	78%	Genet in Med 3:168, 2001;www.dhs.ca.gov/pcfh/gdb/html/PDE/CFStudy.htm
Jewish, non-Ashkenazi		Varies by country of origin	Genet Testing 5:47, 2001, Genet Testing, 1:35, 1997
Other or Mixed Ethnicity		Not Provided	Detection rate not determined and varies with ethnicity

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

METHOD / LIMITATIONS:

DNA is isolated from the sample and tested for the 97 CF mutations listed. 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

athena diagnostics
Four Biotech Park • 377 Plantation Street
Worcester, Massachusetts 01605
(800) 394-4493 • (508) 756-2886

www.AthenaDiagnostics.com
Visit our website for more information on our neurodiagnostic testing services.

Diagnosis Service Report

Patient: DONOR,6739
Sex: M
Social Security Number: [redacted]
Specimen Type: Whole Blood
Test Category: Carrier
Test Requested: SMA Evaluation

Requesting Physician:
Report to: Labcorp V#31982 San Diego/Attn: Referrals
Address: 13112 Evening Creek DR S
Suite 200
San Diego, CA 92128
Additional Reports to:

Accession Number: [redacted]
Family Number/Kindred Number:
[redacted]
Specimen Collection Date: 09/09/2010
Accession Date: 09/11/2010
Report Date: 09/24/2010

Interpretation

This test detected a **normal** copy number of the *SMN1* gene and therefore this individual is unlikely to be a carrier for Spinal Muscular Atrophy (SMA).

RESULTS REVIEWED BY CP
DISCUSSED WITH: RECIPIENT DONOR NA
OK TO FILE Y N
DATE: 10/8/10

Technical Results

SMN1: 2 copies
SMN2: 2 copies

Comments

Carrier Risk for Individuals with no family history of SMA [9]

	Carrier Detection Rate	*Carrier Risk by Ethnicity*	*Residual Risk 2 SMN1 copies*	*Residual Risk 3 SMN1 copies*
Caucasian	95%	1:35	1:632	1:3,500
Ashkenazi Jewish	90%	1:41	1:350	1:4,000
Asian	93%	1:53	1:628	1:5,000
African American	71%	1:66	1:121	1:3,000
Hispanic	91%	1:117	1:1,061	1:11,000

Mixed Ethnicity: If ethnicity is mixed or unknown, use the highest residual risk estimates.

It is our understanding that this sample was submitted for Carrier (asymptomatic) testing based on the information provided from the client.

This analysis identified at least two copies of the *SMN1* gene (**normal**). Normal individuals possess two or more copies of the *SMN1* gene, with at least one copy on each chromosome. Depending upon ethnic background, 70-95% of SMA carriers have only one copy of *SMN1*. The finding of two copies significantly reduces the risk that this individual is a carrier of SMA as defined in the table above. The remaining risk of being a carrier is due to point mutations or 2+0 genotype (2 copies of *SMN1* on one chromosome and zero copies the other chromosome), both of which are not detectible with this test.

It is important to note that 2% of individuals with SMA have a mutation that occurred de novo. Typically in these cases, only one parent is an SMA carrier.

Other testing available: Athena Diagnostics offers *SMN1* DNA sequencing. Please contact Athena Client Services at 800-394-4493 if you wish to consult with a laboratory director or genetic counselor regarding these results.

Limitations of analysis: This analysis cannot identify carrier status due to a 2+0 genotype or point mutations.

Background: Spinal Muscular Atrophy (SMA), characterized by progressive muscle weakness due to atrophy of the lower motor neurons in the spinal cord and brain stem, is the second most common lethal

Patient: DONOR,6739
[redacted] Sex: M Social Security Number
Specimen Type: Whole Blood
Test Category: Carrier
Test Requested: SMA Evaluation

Requesting Physician
Report to: Labcorp V#31982 San Diego/Attn: Referrals
Address: 13112 Evening Creek DR S
Suite 200
San Diego, CA 92128
Additional Reports to:

Diagnosis Service Report
Accession Number: [redacted]
Family Number/Kindred Number
[redacted]
Specimen Collection Date: 09/09/2010
Accession Date: 09/11/2010
Report Date: 09/24/2010

autosomal recessive disorder affecting 1 in every 6,000-10,000 live births.[1,2,6,10,11] Of individuals with SMA, approximately 95% possess zero copies of the *SMN1* gene, while the remaining 5% possess one copy of the gene which harbors a sequence mutation.[10,11]

The carrier frequency for SMA varies between 1 in 34 to 1 in 117 of individuals depending on ethnic background.[2,3,6] Carriers are asymptomatic and typically possess a single copy of the *SMN1* gene. However, a minority of individuals are carriers due to point mutations or a 2+0 genotype (2 copies of the *SMN1* gene on one chromosome and 0 copies on the other chromosome).

Normal individuals possess at least two copies of the *SMN1* gene, typically one on each chromosome 5.[2]

SMN2 copy number relevance: SMA is caused by a critical reduction in the total amount of functional SMN protein. Typically 80-90% of SMN protein is derived from *SMN1* genes, while 10-20% is derived from a homologous gene, *SMN2*.[5] Therefore, SMN protein expression is based primarily on *SMN1* gene copy number. Studies show, the phenotype of affected individuals may be modified by the presence of additional copies of *SMN2* genes. An increased number ($\geq$ 3 copies) of *SMN2* genes may be associated with a less severe phenotype of SMA. Conversely, fewer copies of the *SMN2* ($\leq$ 2) may be associated with a severe phenotype of SMA.[4,5,6] Current literature indicates that in the context of a single *SMN1* copy number, the *SMN2* result is not known to influence carrier status.

Methods

Direct testing of *SMN1* and *SMN2* copy number was performed by quantitative dosage analysis of genomic DNA. The quantitative dosage analysis examines exon 7 of each *SMN1* and *SMN2* gene as well as 21 control loci throughout the genome. This accuracy of dosage analysis, as performed here, is greater than 99% accurate.

All test results are reviewed, interpreted, and reported by ABMG certified Clinical Molecular Geneticists.

Abbreviations: SMA (Spinal Muscular Atrophy); SMN (survival motor neuron).

The SMA Evaluation test is covered by U.S. Patent No. 6,080,577.

References

1. Lefebvre S, et al., (1995). Identification and Characterization of a Spinal Muscular Atrophy-Determining Gene. *Cell*, 80: 155-165.

2. Ogino S and Wilson RB, (2004). Spinal muscular atrophy: molecular genetics and diagnostics. *Expert Rev Mol Diagn*, 4(1): 15-29.

3. Cusin V, et al., (2003). Prevalence of *SMN1* deletion and

Diagnosis Service Report

Patient: DONOR,6739
[redacted] Sex: M Social Security Number
Specimen Type: Whole Blood
Test Category: Carrier
Test Requested: SMA Evaluation

Requesting Physician
Report to: Labcorp V#31982 San Diego/Attn: Referrals
Address: 13112 Evening Creek DR S
Suite 200
San Diego, CA 92128
Additional Reports to:

Accession Number: [redacted]
Family Number/Kindred Number
Patient Number: [redacted]
Specimen Collection Date: 09/09/2010
Accession Date: 09/11/2010
Report Date: 09/24/2010

duplication in carrier and normal populations: implication for genetic counseling. *J Med Genet*, 40:e39.

4. Mailman MD, et al., (2002). Molecular analysis of spinal muscular atrophy and modification of the phenotype by *SMN2*. *Genet Med*, 4: 20-26.

5. Swoboda KJ, et al., (2005). Natural History of Denervation in SMA: Relation to Age, *SMN2* Copy Number, and Function. *Ann Neurology*, 57(5): 704-712.

6. http://www.genetests.org SMA GeneReview authored by Prior TW and Russman BS.

7. Hendrickson BC, et al., (2009). Differences in SMN1 allele frequencies among ethnic groups within North America. *J Med Genet*, 46(9): 641-4.

8. Smith M, et al, (2007). Population screening and cascade testing for carriers of SMA. *Eur J Hum Genet*, 15: 759-66.

9. Lunn MR and Wang CH (2008). Spinal Muscular Atrophy. *Lancet*, 371: 2120-2133.

10. Prior, TW. (2008) Carrier screening for spinal muscular atrophy *Genet.Med.* 10: 840-842

11. Prior, TW (2010) Perspectives and diagnostic considerations in spinal muscular atrophy. *Genet. Med.* 12: 145-152

***** *FINAL REPORT* ***** ver 1.0

This test was developed and its performance characteristics determined by Athena Diagnostics, Inc. It has not been cleared or approved by the U.S. Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary. This test is used for clinical purposes and should not be regarded as investigational or for research only. Athena Diagnostics is licensed under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) to perform high complexity clinical testing. Athena Diagnostics has performed assay validation studies and has developed its laboratory protocols and operating procedures in consultation with experts in the field and in accordance with the standards of the National Committee on Clinical Laboratory Standards (NCCLS).

Sat Dev Batish, PhD, FACMG
Senior Laboratory Director

Masamichi Ito, PhD, FACMG
Senior Laboratory Director

Christine M. Stanley, PhD, FACMG
Laboratory Director