



SMN1 Copy Number Analysis

Patient Name: Sample Patient

DOB:

Age:

SSN #:

Gender: Female

City Hospital
1 Main Street
Anywhere, USA

Genzyme Specimen #:10000001

Case #:

Patient ID #: 20000002

Date Collected: 09/08/2008

Date Received: 09/09/2008

Referring Physician: John Doe, MD

Client Lab ID #: 6

Genetic Counselor:

Hospital ID #:

Specimen ID #:

Specimen Type: Peripheral blood

Specimen(s) Received: 2 - Yellow (ACD) 10 ml round bottom tube(s)

Clinical Data: Carrier Test/No family history

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. Other false negative or false positive results may occur for reasons that include genetic variants, blood transfusions, bone marrow transplantation, or erroneous representation of family relationships.

Carrier Frequency and Risk Reductions for Individuals with No Family History of SMA

Ethnicity	Detection Rate ¹	A priori Carrier Risk ¹	Reduced Carrier Risk for 2 copy result	Reduced Carrier Risk for 3 copy result
Caucasian	94.9%	1:35	1:632	1:3,500
Ashkenazi Jewish	90.2%	1:41	1:350	1:4,000
Asian	92.6%	1:53	1:628	1:5,000
Hispanic	90.6%	1:117	1:1061	1:11,000
African American	71.1%	1:66	1:121	1:3,000
Mixed Ethnicities	For counseling purposes, consider using the ethnic background with the most conservative risk estimates.			

METHOD:

Specimen DNA is isolated and amplified by real-time polymerase chain reaction (PCR) for exon 7 of the SMN1 gene and two reference genes. A mathematical algorithm is used to calculate the number of copies of SMN1. Sequencing of the primer and probe binding sites for the SMN1 real-time PCR reaction is performed on all fetal samples, and on samples from individuals with 1 copy of SMN1 on carrier testing, to rule out the presence of sequence variants which could interfere with analysis and interpretation.

REFERENCES:

1. Carrier frequency and detection rate are calculated based on analysis of allele frequencies among > 1000 individuals from each ethnic group noted (Genzyme Genetics, data submitted for publication). 2. Online review of SMA: <http://www.genereviews.org/profiles/sma>

The test was developed and its performance characteristics have been determined by Genzyme. 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.

Electronically Signed by: D. Alexa Sirko-Osadsa, Ph.D., FACMG, on 9/18/2008

Reported by: ES/es

rep-178-v1-1208

Testing performed at Genzyme Genetics 3400 Computer Drive, Westborough, MA 01581 1-800-255-7357

Page 1 of 1