Client: Example Client ABC123
123 Test Drive
Salt Lake City, UT 84108
UNITED STATES

Physician: Doctor, Example

Patient: Patient, Example

DOB	11/13/1983
Gender:	Female
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	01/01/2017 12:34

Spinal Muscular Atrophy (SMA) Copy Number Analysis (Extended TAT as of 11/20/20-no referral available)

ARUP test code 2013436

SMA Copy Number, Specimen	Whole Blood
SMA Copy Number, Symptoms	Unknown
SMA Copy Number, SMN1 Copies	3 copies
SMA Copy Number, SMN2 Copies	1 copy
SMA Copy Number, Linked Variant	Present
SMA Copy Number, Int	See Note

H=High, L=Low, *=Abnormal, C=Critical

Indication for testing was not provided. The following report is based on an assumption that carrier screening is the indication for testing. If this individual is symptomatic, please contact ARUP for a revised report.

Indication for testing: Carrier screening for spinal muscular atrophy (SMA).

Result: Three copies of SMN1 detected.

Interpretation: Three copies of the SMN1 gene were detected by multiplex ligation-dependent probe amplification (MLPA); therefore, this individual's risk to be a carrier of spinal muscular atrophy (SMA) has been reduced but not eliminated. This test is unable to definitely differentiate individuals with two copies of SMN1 on one chromosome and one copy on the other chromosome (2/1, not a carrier) from the rare individuals with three copies of SMN1 on one chromosome and zero on the other (3/0, silent carrier). However, this individual is positive for linked variants that are sometimes associated with two copies of SMN1 on the same chromosome, particularly in certain ethnic groups. Thus, this individual is more likely to have the former of the two genotypes (2/1) but this cannot be determined with certainty. See the table below for ethnicity-specific post-test risk to be a SMA carrier given this result, assuming no family history of SMA. Bayesian statistical analysis is necessary to determine risk for those with a positive family history. Please refer to the background information included in this report for the limitations of this test.

Ethnicity	Carrier Freq	Post-test Carrier Risk
Caucasian	1 in 35	1 in 3500
Ash Jewish	1 in 41	1 in 4000
Asian	1 in 53	1 in 5000
Afr American	1 in 66	1 in 3000
Hispanic	1 in 117	1 in 11000

Reference for the table above:
Hendrickson et al. Differences in SMN1 allele frequencies among ethnic groups within North America. J Med Genet 2009;46:641-644.

1 copy of the SMN2 gene was/were detected by MLPA. In individuals affected with SMA, SMN2 copy number may inversely correlate with disease severity; however, SMN2 copy number cannot predict phenotype with certainty.

Recommendations: Based on this result, patients should be counseled about the limitations of this test and the residual risk of being an SMA carrier.

This result has been reviewed and approved by [redacted]

BACKGROUND INFORMATION: Spinal Muscular Atrophy (SMA) Copy Number Analysis

CHARACTERISTICS: Spinal muscular atrophy (SMA) is the most common lethal genetic disease in children, and is characterized by progressive muscle weakness due to degeneration of the lower motor neurons. Onset ranges from before birth to adulthood and severity is highly variable. Individuals with SMA have no (zero) functioning copies of the SMN1 gene that produces survival motor neuron protein; most (95 percent) have homozygous loss of SMN1 due to deletion or gene conversion, while some (5 percent) have a sequence variant in one remaining copy of SMN1. The SMN2 gene, adjacent and highly homologous to SMN1, produces lower levels of survival motor neuron protein compared to SMN1. Disease severity has been shown to be modified by SMN2 gene copy number in some cases, but phenotype cannot be predicted with certainty. Two variants that are part of a haplotype associated with SMN1 duplication in silent carriers (2 copies of SMN1 on one chromosome with zero copies on the other) are reported as present or not present. The presence of these variants, particularly in Ashkenazi Jews and Asians, increases the likelihood that 2 copies of SMN1 are on the same chromosome but this is not definitive.
INHERITANCE: Autosomal recessive
CAUSE: Pathogenic mutations in the SMN1 gene.
VARIANTS TESTED: For copy number: SMN1(NM_000344.3) exon 7 c.840C and exon 8 c.*239G, and SMN2 (NM_017411.3) exon 7 c.840T. For haplotype associated with SMN1 duplication (silent carriers): SMN1 c.*3+80T>G (rs143838139) and c.*211_*212del (rs200800214).
CLINICAL SENSITIVITY: 95-98 percent in individuals affected with SMA. Detection rate for carrier screening is 95 percent in Caucasians, 94 percent in Ashkenazi Jewish, 93 percent in Asians, 71 percent in African Americans, and 91 percent in Hispanics.
METHODOLOGY: Multiplex probe ligation-dependent amplification (MLPA)
ANALYTICAL SENSITIVITY AND SPECIFICITY: 99 percent.
LIMITATIONS: Diagnostic errors can occur due to rare sequence variations. Single base pair substitutions, small deletions/duplications, regulatory region mutations, and deep intronic mutations will not be detected. This test is unable to determine chromosomal phase of SMN1 or SMN2 copies. Even if the variants associated with SMN1 duplication are detected, the test cannot definitively differentiate individuals with one or more copies of SMN1 on each chromosome from individuals with two or more copies of SMN1 on one chromosome and zero on the other (silent carriers).

Counseling and informed consent are recommended for genetic testing. Consent forms are available online at www.aruplab.com.

Test developed and characteristics determined by ARUP Laboratories. See Compliance Statement C: aruplab.com/CS

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
SMA Copy Number, Specimen	18-176-126868	6/25/2018 9:02:00 AM	6/26/2018 5:36:00 PM	6/29/2018 1:46:00 PM
SMA Copy Number, Symptoms	18-176-126868	6/25/2018 9:02:00 AM	6/26/2018 5:36:00 PM	6/29/2018 1:46:00 PM
SMA Copy Number, SMN1 Copies	18-176-126868	6/25/2018 9:02:00 AM	6/26/2018 5:36:00 PM	6/29/2018 1:46:00 PM
SMA Copy Number, SMN2 Copies	18-176-126868	6/25/2018 9:02:00 AM	6/26/2018 5:36:00 PM	6/29/2018 1:46:00 PM
SMA Copy Number, Linked Variant	18-176-126868	6/25/2018 9:02:00 AM	6/26/2018 5:36:00 PM	6/29/2018 1:46:00 PM
SMA Copy Number, Int	18-176-126868	6/25/2018 9:02:00 AM	6/26/2018 5:36:00 PM	6/29/2018 1:46:00 PM

END OF CHART