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

Physician: Doctor, Example

Patient: Patient, Example

DOB	3/9/2021
Gender:	Female
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	00/00/0000 00:00

Spinal Muscular Atrophy (SMA) Copy Number Analysis

ARUP test code 2013436

SMA Copy Number, Specimen	Whole Blood
SMA Copy Number, Symptoms	No
SMA Copy Number, SMN1 Copies	1 copy *
SMA Copy Number, SMN2 Copies	1 copy
SMA Copy Number, Linked Variant	Not Present
SMA Copy Number, Int	See Note

Indication for testing: Carrier screening for spinal muscular atrophy (SMA).
Result:
SMN1 gene copies: 1
SMN2 gene copies: 1 copy
Linked variant: not detected

Interpretation: One copy of the SMN1 gene was detected by multiplex ligation-dependent probe amplification (MLPA); therefore, this individual is predicted to be at least a carrier of spinal muscular atrophy (SMA). Please refer to the background information included in this report for the clinical sensitivity and limitations of this test.

Recommendations: Genetic counseling is recommended. This individual's reproductive partner and adult family members should be offered SMA carrier screening.

This result has been reviewed and approved by [redacted]

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

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 functioning copies of the SMN1 gene. Most (95 percent) have homozygous loss of SMN1 due to deletion or gene conversion, while a minority (5 percent) have a deletion of SMN1 on one chromosome and a SMN1 sequence variant on the other. 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, though phenotype cannot be predicted with certainty. An SMN1 variant, c.*3+80T>G (rs143838139), that is part of a haplotype associated with SMN1 duplication in silent carriers (two copies of SMN1 on one chromosome and no copies on the other), particularly in Ashkenazi Jews, increases the likelihood that two copies of SMN1 are on the same chromosome.
INHERITANCE: Autosomal recessive.
CAUSE: Pathogenic variants 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).
CLINICAL SENSITIVITY: 95-98 percent in individuals affected with SMA. Detection rate for carrier screening is 90 percent in African Americans, 93 percent in Ashkenazi Jewish, 93 percent in Asians, 95 percent in Caucasians, and 93 percent in Hispanics.
METHODOLOGY: Multiplex ligation-dependent probe amplification (MLPA) to detect SMN1 and SMN2 copy number and presence or absence of the SMN1 linked variant c.*3+80T>G (rs143838139).
ANALYTICAL SENSITIVITY AND SPECIFICITY: 99 percent.
LIMITATIONS: Diagnostic errors can occur due to rare sequence variations. Single base pair substitutions, small deletions/duplications, and regulatory region and deep intronic variants will not be detected. SMN2 copy numbers greater than 3 may not be reliably distinguished. This test is unable to determine chromosomal phase of SMN1 or SMN2 copies. Even if the linked variant associated with SMN1 duplication is detected, the test cannot definitively differentiate between 1+ copies of SMN1 on each chromosome from 2+ copies of SMN1 on one chromosome and none on the other (silent carriers).

This test was developed and its performance characteristics determined by ARUP Laboratories. It has not been cleared or approved by the U.S. Food and Drug Administration. This test was performed in a CLIA- certified laboratory and is intended for clinical purposes.

Counseling and informed consent are recommended for genetic testing. Consent forms are available online.

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
SMA Copy Number, Specimen	25-069-107252	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
SMA Copy Number, Symptoms	25-069-107252	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
SMA Copy Number, SMN1 Copies	25-069-107252	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
SMA Copy Number, SMN2 Copies	25-069-107252	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
SMA Copy Number, Linked Variant	25-069-107252	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
SMA Copy Number, Int	25-069-107252	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00

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