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PATIENT REPORT

Patient Age/Sex: 31 years Female

Specimen Collected: 04-Sep-23 17:22

Spinal Muscular Atrophy(SMA) Copy Number | **Received: 05-Sep-23 17:23** | **Report/Verified: 05-Sep-23 17:26**

Procedure	Result	Units	Reference Interval
SMA Copy Number,Specimen	Whole Blood		
SMA Copy Number,Symptoms	No		
SMA Copy Number,SMN1 Copies	**1 copy** *		
SMA Copy Number,SMN2 Copies	2 copies		
SMA Copy Number,Linked Variant	Not Present		
SMA Copy Number,Int	See Note f1 i1		

Result Footnote

f1: SMA Copy Number, Int

Section 79-1 of New York State Civil Rights Law requires informed consent be obtained from patients (or their legal guardians) prior to pursuing genetic testing. These forms must be kept on file by the ordering physician. Consent forms for genetic testing are available at www.aruplab.com. Incidental findings are not reported unless clinically significant but are available upon request.

Indication for testing: Carrier screening for spinal muscular atrophy (SMA).
Result:
SMN1 gene copies: 1
SMN2 gene copies: 2 copies
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]

Test Information

i1: SMA Copy Number, Int

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 (2 copies of SMN1 on one chromosome and no copies on

Test Information

i1: SMA Copy Number, Int

the other), particularly in Ashkenazi Jews, increases the likelihood that 2 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 probe ligation-dependent 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. 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 US 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.