MedGenome Labs Limited.
Sy No 94/1C and 94/2, Tower-1,
Veerasandra Village, Attibele Hobli,
Electronic City, Phase-1,
Bangalore, Karnataka, 560100.
Tel: +91 (0)80 67154932 / 933

MEDGENOME

DNA TEST REPORT – MEDGENOME LABORATORIES

Full Name / Ref No:	**Kishan N**	Order ID/Sample ID:	**1548955/9600813**
Date of Birth / Age:	1 Year	Gender:	Male
Parental Sample ID:	NA	Sample Type:	Peripheral Blood in EDTA (Purple Top)
Referring Clinician:	Dr. Ann Agnes Mathew Virgo Healthcare Bengaluru	Date of Sample Collection:	NA
		Date of Sample Receipt:	6th December 2025
		Date of Order Booked:	6th December 2025
		Date of Report:	15th December 2025
Test Requested:	**Spinal Muscular Atrophy (*SMN1/SMN2*) deletion/duplication analysis [MGM2540]**		

CLINICAL DIAGNOSIS / SYMPTOMS / HISTORY

The patient, born of non-consanguineous marriage, presented with clinical indications of upper and lower limb weakness, peripheral hypotonia, proximal and distal weakness. The patient is being evaluated for pathogenic deletions and duplications in exons 7 and 8 of *SMN1* and *SMN2* genes.

RESULTS*

PATHOGENIC VARIANT CAUSATIVE OF THE SUSPECTED PHENOTYPE WAS IDENTIFIED

Sl. No.	Gene Exons‡	Deletions /Duplications	MLPA probe ratio (Dosage quotient)#	Copy number	Disease (OMIM)	Inheritance	Classification
1	*SMN1* (Exon 7)	Homozygous deletion	Exon 7 (0.00)	0	Spinal muscular atrophy	Autosomal recessive	Pathogenic
2	*SMN1* (Exon 8)		Exon 8 (0.00)	0			
3	*SMN2* (Exon 7)		Exon 7 (0.93)	2	-	-	-
4	*SMN2* (Exon 8)		Exon 8 (0.99)	2			

CLINICAL CORRELATION AND VARIANT INTERPRETATION

Homozygous deletion of exons 7 and 8 in the *SMN1* gene was detected within the detection limits of MLPA**,** in the subject (Fig.1). No deletion or duplication was detected of exons 7 and 8 in *SMN2* gene. The subject has gene copy number ratio of *SMN1*:*SMN2* of 0:2. Functional absence of *SMN1* gene due to homozygous deletions is reported to be pathogenic in 95% of SMA cases [1]. Hence, **this deletion is pathogenic and must be carefully correlated with clinical symptoms.**

RECOMMENDATIONS

Genetic counselling is advised.

Screening of parents is recommended to determine their carrier status.

CAP ACCREDITED
COLLEGE of AMERICAN PATHOLOGISTS

MedGenome Labs Limited.
Sy No 94/1C and 94/2, Tower-1,
Veerasandra Village, Attibele Hobli,
Electronic City, Phase-1,
Bangalore, Karnataka, 560100.
Tel: +91 (0)80 67154932 / 933

BACKGROUND

Spinal muscular atrophy (SMA) is characterized by degeneration of lower motor neurons in the spinal cord, causing progressive paralysis of the limbs and trunk, followed by muscle atrophy. SMA is one of the most frequent autosomal recessive diseases, with a carrier frequency of 1 in 38 and is the most common genetic cause of childhood mortality [4]. The phenotype is extremely variable, and patients are classified as SMA type I to III based on age at onset and clinical course. There are two (highly similar) genes playing a pivotal role in SMA: *SMN1* and *SMN2*. These two genes can only be distinguished by single nucleotide differences in exon 7 and 8. *SMN2* is much less efficient in making the SMN protein; therefore, it is the *SMN1* gene which is the determinant factor in SMA. Of these, greater than 96% are homozygous for the deletion of exons 7 and 8 of this gene. Genetic analysis for this deletion provides an efficient diagnosis for this disorder.

TEST METHODOLOGY

Copy number changes in exons 7 and 8 of the *SMN1* & *SMN2* genes were identified by hybridizing with MLPA (Multiplex Ligation-dependent Probe Amplification) probes. Each MLPA probe consists of two hemi-probes that bind to adjacent sites on the target sequence. Upon ligation and subsequent PCR amplification, each distinct MLPA probe (specific to distinct target regions) generates an amplicon with a unique length which is separated and quantified by capillary electrophoresis. Heterozygous deletions within target sequences will prevent efficient probe binding and give a 35-50% reduced relative peak area of the amplification product specific to that probe set. Copy number differences of various exons between test and control DNA samples can be detected by analyzing the MLPA peak patterns.

***Genetic test results are reported based on the recommendations of American College of Medical Genetics (Richards CS et al., Genet Med, 2015), as described below:**

Variant	A change in a gene. This could be disease causing (pathogenic) or not disease causing (benign).
Pathogenic	A disease-causing variation in a gene which can explain the patients' symptoms has been detected. This usually means that a suspected disorder for which testing had been requested has been confirmed.
Likely Pathogenic	A variant which is very likely to contribute to the development of disease, however, the scientific evidence is currently insufficient to prove this conclusively. Additional evidence is expected to confirm this assertion of pathogenicity.
Benign	A variant which is known not to be responsible for disease has been detected. Generally, no further action is warranted on such variants when detected.
Likely Benign	A variant is not expected to have a major effect on disease however, the scientific evidence is currently insufficient to prove this conclusively. Additional evidence is expected to confirm this assertion.
Variant of Uncertain Significance	A variant has been detected, but it is difficult to classify it as either pathogenic (disease causing) or benign (non-disease causing) based on current available scientific evidence. Further testing of the patient or family members as recommended by your clinician may be needed. It is probable that their significance can be assessed only with time, subject to availability of scientific evidence.

‡ the exon numbering is based on the *SMN1* mRNA reference sequence NM_000344.3 and *SMN2* mRNA reference sequence NM_017411.3 nomenclature respectively in the NCBI GenBank database.

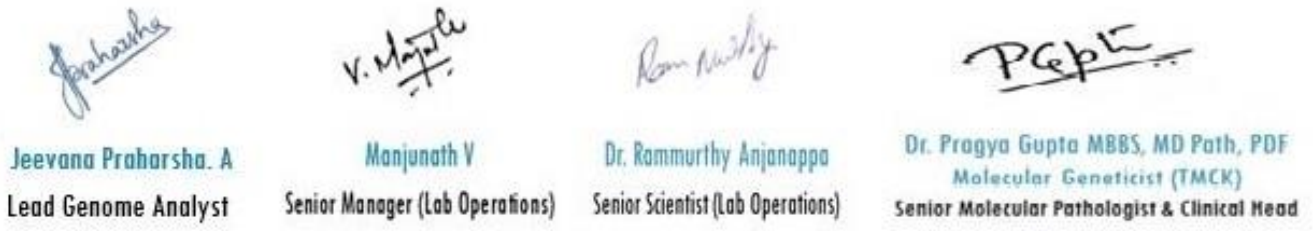
MLPA ratios (dosage quotient) of below 0.7 or above 1.3 are indicative of a deletion (copy number change from two to one) or duplication (copy number change from two to three), respectively. A dosage quotient of 0.0 indicates a homozygous deletion, 0.35 to 0.65 indicates heterozygous deletion, 1.35 to 1.55 indicates heterozygous duplication and 1.7 to 2.2 indicates homozygous duplication. A MLPA ratio (dosage quotient) between 0.80 to 1.20 indicates a normal copy number status

MedGenome Labs Limited.
Sy No 94/1C and 94/2, Tower-1,
Veerasandra Village, Attibele Hobli,
Electronic City, Phase-1,
Bangalore, Karnataka, 560100.
Tel: +91 (0)80 67154932 / 933

MEDGENOME

DISCLAIMER

- MLPA cannot detect any changes that lie outside the target sequence of the probes and will not detect most inversions or translocations. Even when MLPA did not detect any aberrations, the possibility remains that biological changes in that gene or chromosomal region do exist but remain undetected.
- The MLPA test will not detect the point mutations in the *SMN1* and *SMN2* genes.
- A point mutation or polymorphism in the sequence detected by a probe, which results in reduced probe binding efficiency, can also cause a reduction in relative peak area. Therefore, single exon deletions detected by MLPA should always be confirmed by other methods like multiplex PCR or sequencing.



REFERENCES

1. Yoon S, Lee CH, Lee KA. Determination of *SMN1* and *SMN2* copy numbers in a Korean population using multiplex ligation-dependent probe amplification. Korean J Lab Med. 2010; 30(1):93-6.
2. Ogino S, Wilson RB. Spinal muscular atrophy: molecular genetics and diagnostics. Expert Rev Mol Diagn. 2004;4(1):15-29.
3. Prior TW et al, Homozygous *SMN1* deletions in unaffected family members and modification of the phenotype by *SMN2*. Am J Med Genet A. 2004.
4. Nilay M, Moirangthem A, Saxena D, Mandal K, Phadke SR. Carrier frequency of SMN1-related spinal muscular atrophy in north Indian population: The need for population-based screening program. Am J Med Genet A. 2021 Jan;185(1):274-277. doi: 10.1002/ajmg.a.61918. Epub 2020 Oct 14. PMID: 33051992.

CAP ACCREDITED
COLLEGE of AMERICAN PATHOLOGISTS

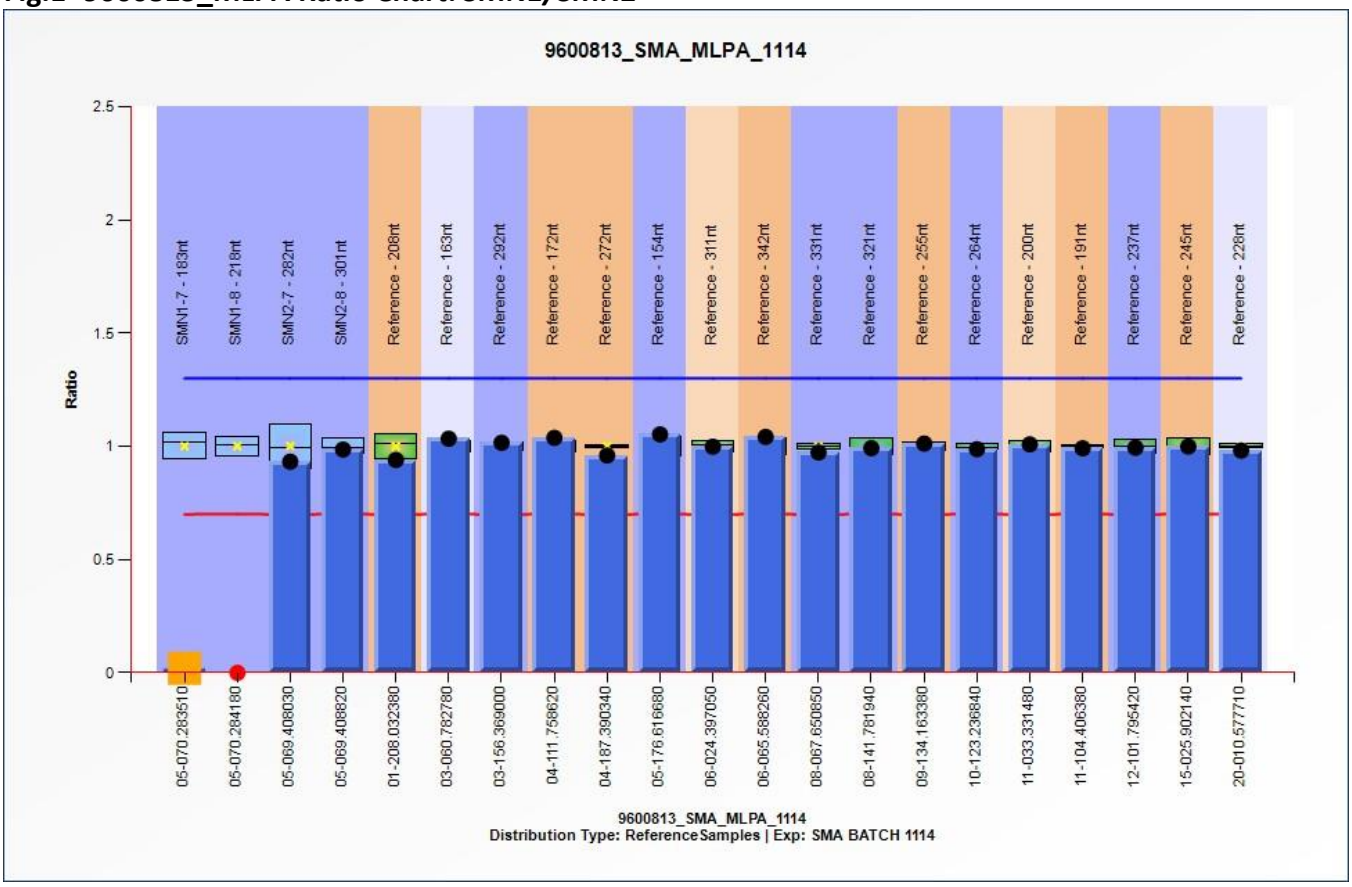
MedGenome Labs Limited.
Sy No 94/1C and 94/2, Tower-1,
Veerasandra Village, Attibele Hobli,
Electronic City, Phase-1,
Bangalore, Karnataka, 560100.
Tel: +91 (0)80 67154932 / 933

MEDGENOME

APPENDIX-1e

SMN1/SMN2 -MLPA Result Figure

Fig.1- 9600813_MLPA Ratio Chart: *SMN1/SMN2*



……End of Report……

CAP ACCREDITED
COLLEGE of AMERICAN PATHOLOGISTS