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International assessment of newborn screening for spinal muscular atrophy using advanced sequencing and artificial intelligence

Maria del carmen Garrido[1 2 3],Teresa Martínez de Filartiga[4],Rubén Darío Duré[4], Ruth Zárate[5], Marco Casartelli[6], Marija Chaushevska[2,7]Gjorgji Madjarov,[2,7] Zoran Velkoski[2]and Chris Kyriakidis.[2]

[1]CONGEN, Genetic Counselling Services, Granada, Spain; [2]gMendel ApS, Copenhagen, Denmark; [3]Cardiovascular Development Group, Department of Experimental Biology, University of Jaen, Spain; [4]Laboratorio Curie, Asunción, Paraguay; [5]GT-Scientific S.A., Asunción, Paraguay; [6]Programa Nacional de Detección Neonatal. Ministerio de Salud Pública y Bienestar Social, Asunción,Paraguay; [7]University of Ss.Cyril & Methodius, Macedonia, North Macedonia.

DISCLAIMER: The authors declare no confilct of interest

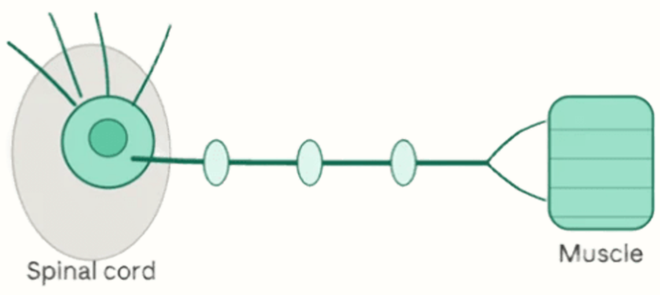
Contact

BACKGROUND

SMA is an autosomal recessive neuromuscular disease (1/10,000 births) caused by homozygous deletions in *SMN1* exon 7.

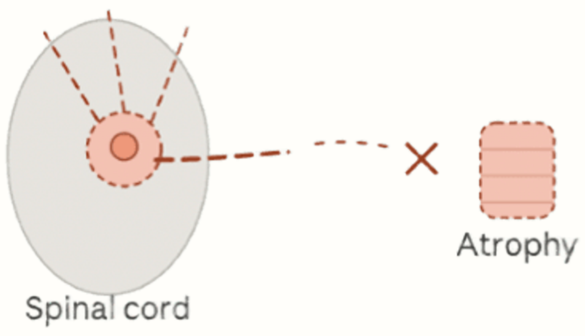
Clinical severity is modulated by *SMN2* copy number. Early diagnosis is critical: disease-modifying therapies are available, and newborn screening (NBS) enables presymptomatic identification.

Healthy
SMN1 intact · functional protein



SMN protein → motor neuron survival → normal muscle function.

SMA
SMN1 exon 7 deleted · no functional protein



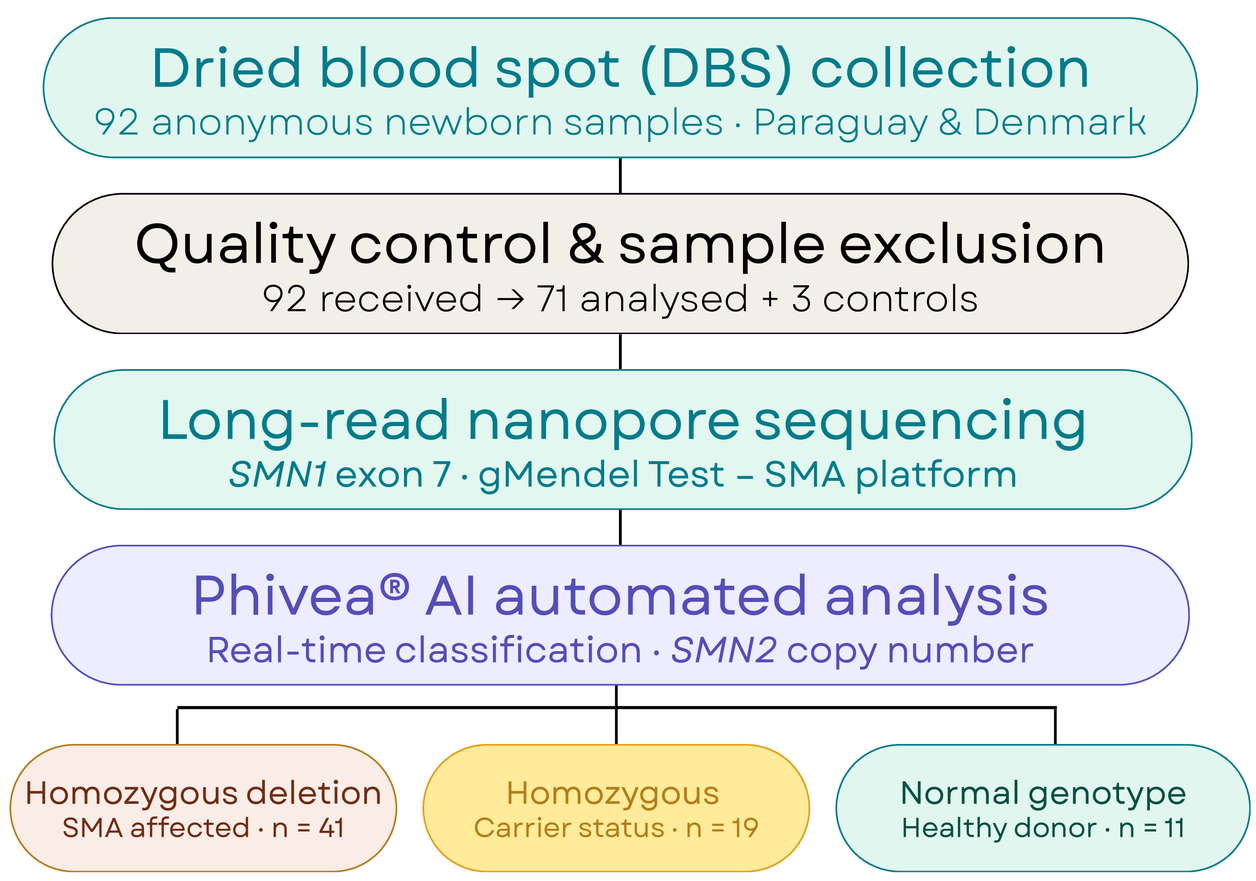
Loss of SMN protein → motor neuron degeneration → progressive weakness

Early presymptomatic diagnosis via NBS enables treatment before irreversible motor neuron loss

MATERIAL AND METHODS:

As part of a pilot study conducted in collaboration with Paraguay and Denmark, 92 anonymous dried blood samples were received. After excluding low-quality samples, 71 samples (41 diagnosed SMA cases, 19 carriers, and 11 healthy donors) were analysed along with 3 controls.

The Phivea® platform (gMendel Test - SMA), based on long-read sequencing and artificial intelligence (AI), was used. The analysis allowed classification of samples into homozygous deletion of *SMN1* exon 7, heterozygous status, or normal genotype, and the number of SMN2 copies was also assessed.



RESULTS:

100%
Analytical sensitivity
No SMA case missed

96.8%
Analytical specificity
Very low false-positive rate

98.6%
Overall accuracy Across all 71 samples

97.6%
Diagnostic sensitivity Clinical confirmation

100%
Diagnostic specificity Zero false positives

0.024
Negative likelihood ratio
Excellent rule-out power

CONCLUSION:

The gMendel-SMA test demonstrates high robustness and reliability for population-based NBS. International collaboration between Spain, Paraguay, Denmark and North Macedonia confirms its feasibility in resource-limited settings.

ESHG European Human Genetics Conference