AI cloud-based end-to-end technology for accurate, fast & affordable diagnosis for Spinal Muscular Atrophy in Paraguay

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Abstract

Spinal Muscular Atrophy (SMA), a progressive, recessive neuromuscular disease with varying presentations of onset and severity, is caused by bi-allelic mutations in the *SMN1* gene (deletion of the gene in 95% of the cases). The severity is determined by the number of *SMN2* copies. *SMN1* and *SMN2* only have 5 different nucleotides in the whole sequence. Due to its high clinical and genetic heterogeneity and low prevalence (1/10,000 births), diagnosis and treatment are highly challenging.

Genetic diagnosis is usually made using RT-PCR for *SMN1* (and sometimes *SMN2*) after clinical symptoms suggest the condition. This procedure is costly, slow, and inefficient, as many of the clinical symptoms overlap with other neuromuscular diseases (DMD, BMD, or multiple sclerosis), increasing the misdiagnosis rate.

Our proposed solution combines targeted ONT sequencing and our Phivea® platform to discriminate between *SMN1* and *SMN2*, ascertain the number of copies per gene, and identify a point mutation (C>T) typically occurring in the telomeric region.

Materials and Methods

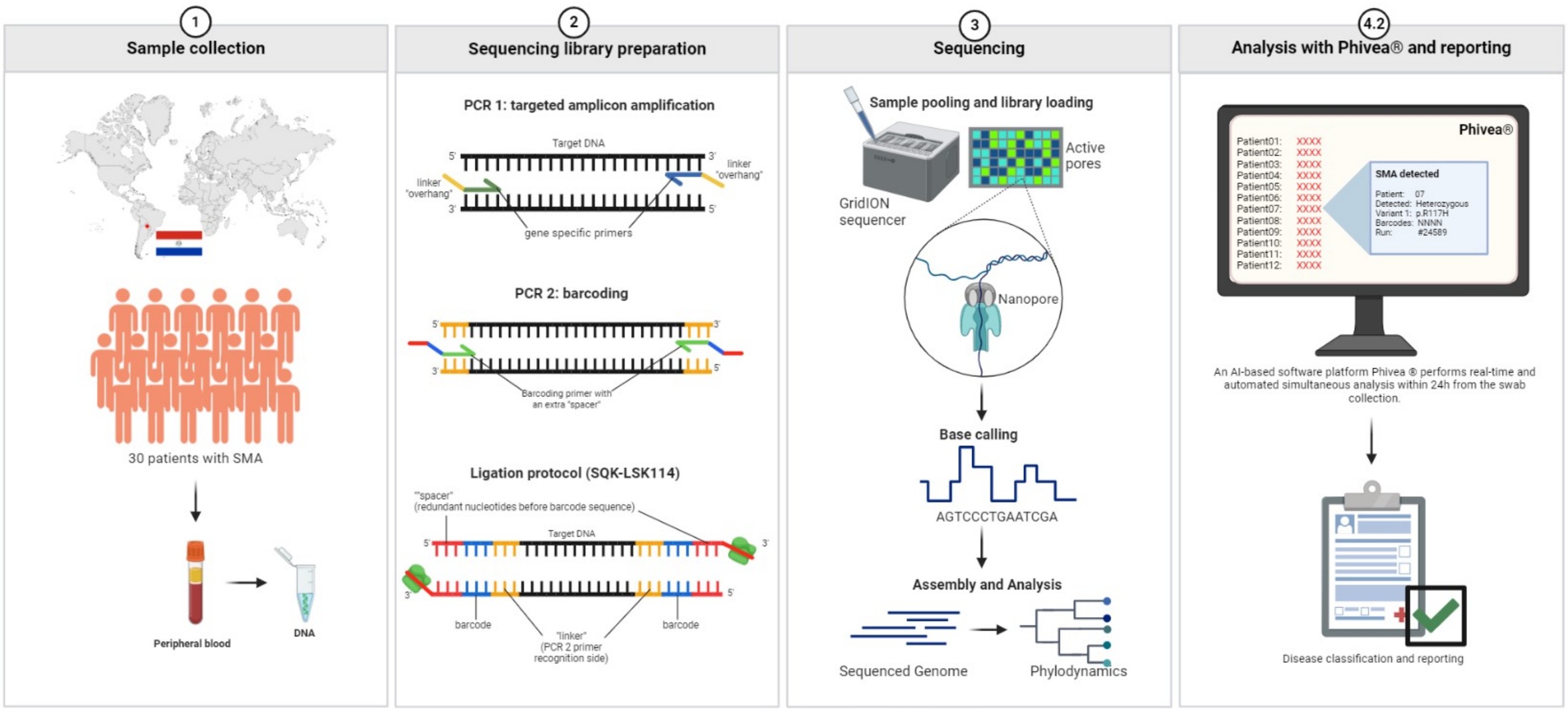
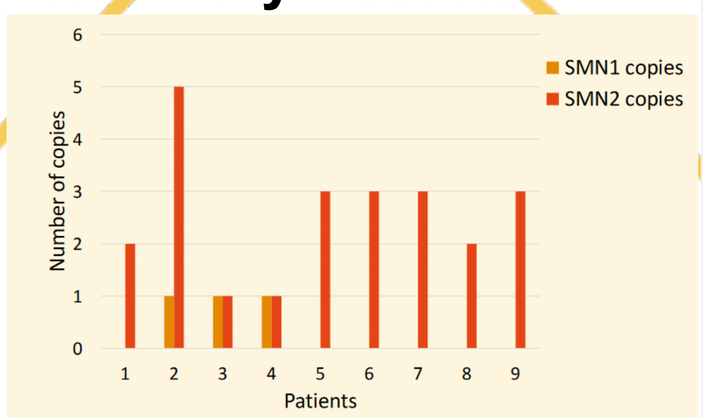


Figure 1: End-to-end assay.

Thirty samples were collected from SMA patients in Paraguay for this pilot study. Sequencing library preparation involved PCR1, targeting DNA amplification from intron 6 to exon 8 for *SMN1* and *SMN2* using specific primers, alongside amplification of an endogenous control. PCR2 was conducted for barcode attachment and library preparation. Nanopore sequencing was performed by loading the library onto a Flowcell FLO-MIN106 (R9.4.1) and sequencing with GridION x5 (ONT). Real-time data analysis utilized Phivea® for multilevel demultiplexing and tailor-made real-time data analysis.

Preliminary Results



Patient	1	2	3	4	5	6	7	8	9
SMN1	0	1	1	1	0	0	0	0	0
SMN2	2	5	1	1	3	3	3	2	3
Result	SMA	Carrier	Carrier	Carrier	SMA	SMA	SMA	SMA	SMA

In a preliminary study in which we applied the technology, we were able to effectively discriminate between *SMN1* and *SMN2* genetic variants based on the five different nucleotides. The results obtained were consistent with reports from the Coriell Institute for Medical Research, thus validating the robustness of our approach. In addition, it was concluded that *SMN2* copy number determination provides a valuable indicator for diagnosis, as higher copy number correlates with lower disease severity.

Conclusion

- The Phivea® platform can be used as a novel automated approach to study *SMN1* and *SMN2* mutations to improve the diagnostic yield of SMA.

- By automating the process and utilizing artificial intelligence, this platform could potentially reduce both the time and cost involved in diagnosing SMA.

- gMendel® is the only end-to-end IVD certified technology with real-time data analysis, with hundreds of samples simultaneously analysed in <24 hrs through a novel combination of genomics & AI.

For more information, contact carmen@g-mendel.com or at www.g-mendel.com