AI cloud-based end-to-end technology for accurate, fast & affordable diagnosis of genetic disorders in Egypt

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Abstract

Different technologies are used to diagnose genetic disorders depending on the genetic alteration. For chromosomal abnormalities such as Klinefelter syndrome (KS) or Turner syndrome (TS), karyotyping/FISH/microarrays are used although the resolution is limited for small chromosomal rearrangements and mosaicism. For point mutations such as cystic fibrosis (CF), standard NGS is performed after a clinical suggestion by sweat chloride test (SCT). Finally, diagnosis of spinal muscular atrophy (SMA) caused by bi-allelic mutations in the SMN1 is diagnosed by RT-PCR for mutations in *SMN1* and for copy number of *SMN2*.

The need to use diverse methodologies in a disease-dependent case is suboptimal in newborn screening approaches.

Our proposed solution combines targeted ONT sequencing and our Phivea® platform to detect chromosomal aneuploidies, point mutations and copy number alterations, being suitable as a screening tool for SMA, CF, KS & TS among other potential genetic disorders.

Materials and Methods

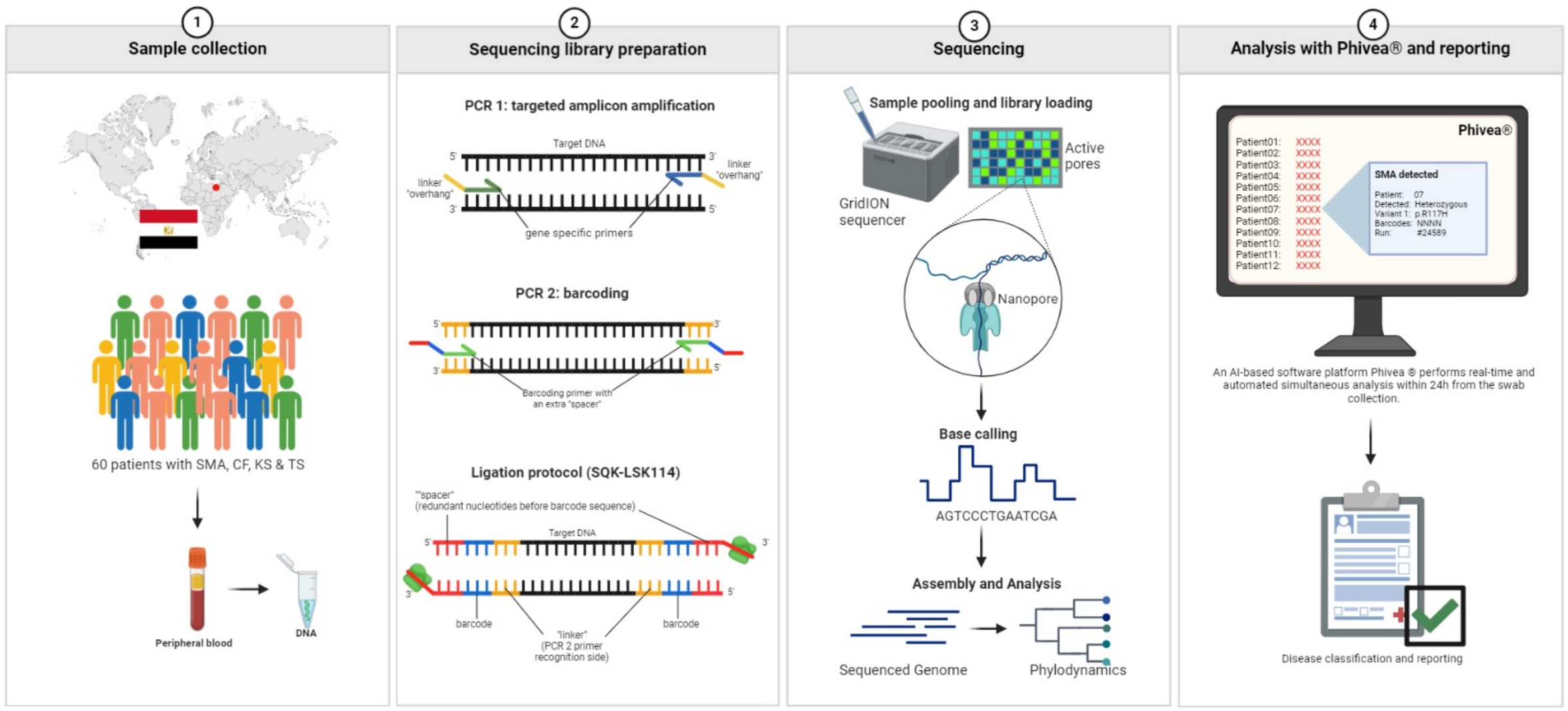

Figure 1: End-to-end assay.

Sixty samples to be collected from patients with SMA, CF, KS & TS in Egypt for this pilot study. Sequencing library preparation involves PCR1, targeting DNA amplification using specific primers. PCR2 is conducted for barcode attachment and library preparation. Nanopore sequencing is performed by loading the library onto a Flowcell FLO-MIN106 (R9.4.1) and sequencing with GridION x5 (ONT). Real-time data analysis utilizes Phivea® for multilevel demultiplexing and tailor-made real-time data analysis.

Preliminary Results

In various preliminary studies where we applied the technology, we successfully discriminated between SMN1 and SMN2 genetic variants based on five different nucleotides and diagnosed CF, KS, & TS. The results aligned with reports from the Coriell Institute for Medical Research, validating the robustness of our technology. Phivea® effectively detected the most common mutations of the CFTR gene and differentiated between carriers and CF-affected patients. Furthermore, it accurately identified CF, SMA, and FXS, along with adult carriers from all affected ethnicities, achieving sensitivity and specificity levels exceeding 90% and an accuracy rate of 100%.

Phivea® RESULTS	
Metric	Value
Analysis Throughput (reads per second)	4120
Correct Identification of Genetic Disorders - Cystic Fibrosis (CF) - Spinal Muscular Atrophy (SMA) - Fragile X Syndrome (FXS)	 YES YES YES
Sensitivity*	>90%
Specificity *	>90%
Accuracy**	100%

Table 1: Preliminary study results of the Phivea® application for CF, SMA and FXS.

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

Table 2: Preliminary study results of the Phivea® application for SMA.

		TOTAL	Heterozygous	Homozygous	Type of variations	
CFTR mutation variation	f508del	9	6	3	-	
	W1282X	2	2	-	G/A	
	p.R347P	2	2	-	C/G	G/A
	p.R347H	2	2	-	C/G	G/A
	621+1G>T	3	3	-	G/T	

Table 3: Preliminary study results of the Phivea® application for CF.

Conclusions

- We developed an AI-powered, vertically-integrated IVD certified technology with real-time data analysis, with hundreds of samples simultaneously analysed in <24 hrs through a novel combination of genomics & AI.
- There is an opportunity to substitute older diagnostic tools with more accurate, faster & cost-effective technology, helping to prevent lifelong costly treatment and human suffering.
- Our Companion Diagnostics as a Service can accelerate the diagnostic journey towards precision treatments or clinical trials and advances inclusion, diversity and equity in care and treatment.

For more information
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