ULTRA-PORTABLE NANOPORE SEQUENCING WITH ADAPTIVE SAMPLING FOR CLINICAL DIAGNOSTICS:

PRELIMINARY EVALUATION USING MONOGENIC DIABETES AS A MODEL

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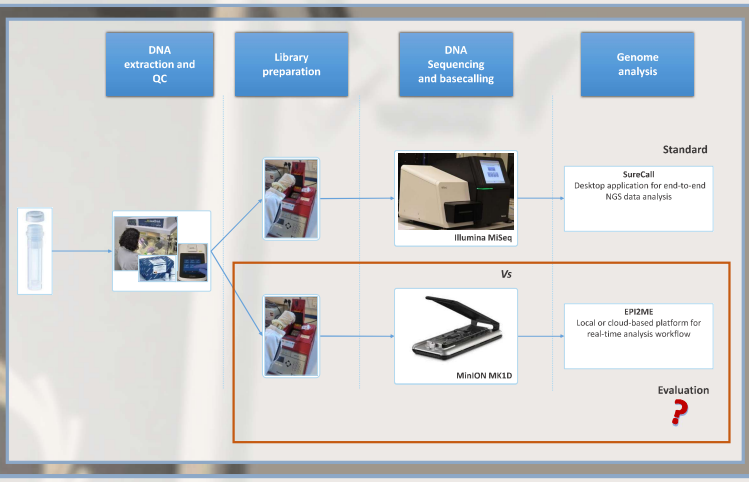
Introduction

Next-generation sequencing (NGS) has become integral to modern clinical genetics, revolutionizing our capacity for molecular diagnosis. Among emerging technologies, Oxford Nanopore sequencing presents compelling advantages for clinical applications, including rapid turnaround times, exceptional portability, and the potential for point-of-care diagnostics.

The ONT MinION platform represents a paradigm shift in this context, enabling ultra-portable, real-time genetic analysis beyond traditional laboratory infrastructures. Its compact design and operational flexibility facilitate deployment in diverse settings, from routine clinical environments to resource-constrained regions and emergency response scenarios. Furthermore, the adaptive sampling functionality enables selective enrichment of genomic regions of interest, supporting targeted diagnostics in situ.

This work is conducted within the framework of project "Implementation of a Blueprint for Mobile Genetic Diagnostics: Nanopore Sequencing of Monogenic Diabetes Genes as a Model for Genetic Analysis", and we present here the first results from this initiative. Our objective is to validate the implementation of the MinION MK1D device coupled with a standard laptop configuration, aiming to democratize access to genetic testing for rare diseases in challenging operational contexts where conventional sequencing infrastructure may be limited or unavailable.

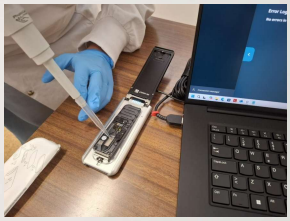


Our aim:
Implementation of the MinION Nanopore sequencer with a standard laptop to expand access to genetic testing, particularly for rare diseases, in challenging contexts.

Methods

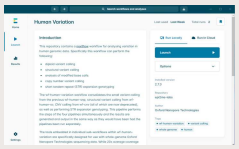
DNA from 16 samples
(previously sequencing for GCK, HNF1A, HNF1B and HNF4A)

Rapid DNA barcoding
with Nanopore Rapid Barcoding Kit 24 - RBK114.24



Nanopore sample preparation
minION MK1D with Nanopore Flow Cell R10 version

Samples run
with Nanopore MinKNOW software using adaptive sampling for monogenic diabetes genes



Analysis with Nanopore EPI2ME software

Results

Sequencing data were successfully generated for all samples across the targeted diabetes gene panel, demonstrating the technical feasibility of the MinION MK1D setup. However, the average sequencing depth achieved was 2–3×, which falls below the threshold typically recommended for confident variant calling in clinical diagnostics. Despite this limitation, all samples yielded interpretable data, allowing for preliminary variant detection and assessment.

These findings indicate that while the current configuration shows promise for portable genetic testing, several aspects require optimization before implementation in point-of-care settings. Key areas for improvement include increasing sequencing depth through extended run times or optimized library preparation protocols, and enhancing computational resources to support real-time basecalling and variant analysis. With these refinements, the platform has the potential to deliver clinically actionable results in resource-limited environments, thereby expanding access to molecular diagnostics for rare disease investigation.

Discussion

Our results demonstrate the technical feasibility of deploying the MinION platform in a highly portable configuration for targeted genetic testing. While the sequencing depth achieved (2–3×) limits robust clinical variant calling, these findings represent an important proof-of-concept for this approach. The platform's key advantages—portability, real-time data acquisition, and adaptive sampling—remain evident despite current coverage limitations. The ability to generate interpretable data using a laptop-based system represents a significant step toward democratizing molecular diagnostics in settings where conventional infrastructure is unavailable.

Several optimization strategies are expected to improve performance substantially: refinement of panel design and enrichment protocols, workflow optimization including library preparation modifications, enhanced computational resources for real-time processing, and extended sequencing runs or multiplexing to achieve clinically adequate depth (typically ≥20×).

With systematic implementation of these improvements, this platform has the potential to deliver clinically actionable results in decentralized settings, particularly for rare disease diagnostics in remote regions, resource-limited environments, and situations requiring rapid turnaround. Future work will focus on validating these optimizations and establishing quality benchmarks for point-of-care applications.

References

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