

# Comprehensive characterisation of cancer predisposition genes using the Hereditary Cancer Panel

Hereditary cancers account for ~5–10% of diagnosed cancers and are caused by inherited abnormalities in genes that lead to defects in cellular pathways, such as in DNA repair or cell cycle regulation<sup>1</sup>. Accurate detection of inherited mutations in cancer predisposition genes is important for clinical management of patients and their relatives<sup>2</sup>. Current germline genetic testing relies on clinical criteria, such as tumour type, age of onset, and family history, to select genes to assay<sup>3</sup>. Often, genetic testing begins with analysis of a single specific high-risk gene, such as *BRCA*, or a small set of idiopathic genes. Sometimes, if the genetic variant remains unknown, larger, more comprehensive assays may be employed<sup>4</sup>, for example, large target enrichment panels or whole-genome sequencing. In addition, many of these current methods rely on short-read sequencing, which often cannot adequately resolve complex structural variants (SVs), intronic regions, and epigenetic modifications, further limiting diagnostic yield.

Oxford Nanopore sequencing overcomes these limitations by generating reads of unrestricted length, enabling the easy resolution of complex and repetitive regions. Plus, leveraging high-accuracy direct sequencing of native DNA, epigenetic modifications are captured, allowing the analysis of all genetic and epigenetic variants in one go, something that is not possible with legacy technologies. Furthermore, Adaptive Sampling, a targeted sequencing method unique to Oxford Nanopore, provides real-time, on-device enrichment of regions of interest without the need for baits or probes.

The Hereditary Cancer Panel uses Oxford Nanopore sequencing to provide comprehensive characterisation of 258 full-length genes implicated in hereditary cancer predisposition, including introns and promoters. This workflow provides a simple and targeted approach for investigating hereditary cancers, consolidating multiple assays into a single workflow. By harnessing Adaptive Sampling, achieve enhanced detection of single nucleotide variants (SNVs) and small indels, and improve characterisation of SVs, pseudogenes, and repetitive regions across targeted areas without additional library preparation. Plus, detect copy number variation with low-pass whole-genome coverage. Streamline your precision oncology research with this scalable, accessible, and cost-effective method.

Here we present a streamlined targeted sequencing method to comprehensively characterise 258 genes associated with cancer predisposition using high-output PromethION™ Flow Cells.

## Sample preparation: extracting and preparing your samples for sequencing

Learn more about Oxford Nanopore library preparation:  
[nanoporetech.com/prepare](https://nanoporetech.com/prepare)

The Hereditary Cancer Panel is available as a bundle, with options for 18 or 72 samples, providing all Oxford Nanopore consumables and reagents needed for library preparation.

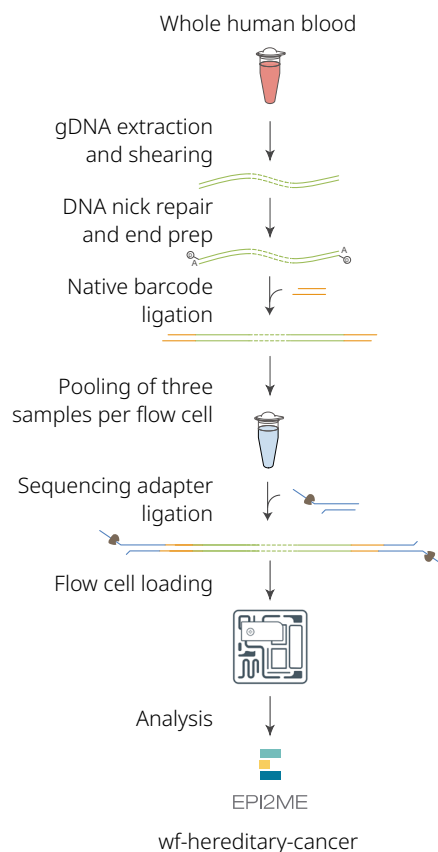
Starting with whole human blood, extract DNA using the **QIAGEN Puregene Blood Kit** before shearing with a **Covaris g-TUBE** to ensure the extracted DNA is of uniform length (~7.5–8.5 kb).

Next, prepare the extracted DNA for sequencing with the **Native Barcoding Kit**, a high-throughput library preparation kit, which barcodes samples for multiplex sequencing. This is a PCR-free kit, preserving long fragments and epigenetic modifications of native DNA for direct sequencing.

During library preparation, repair any nicks in the DNA and prepare the ends for barcode attachment. Select a unique barcode for each sample that will be sequenced in a multiplex of three. We recommend processing samples in increments of three as the protocol has been optimised to sequence three samples per PromethION Flow Cell. Whilst the samples are separate, ligate the native barcodes to the DNA ends and then pool three samples together.

To prepare your pooled samples for sequencing, ligate the sequencing adapters to the DNA ends. Next, the flow cell is primed and the library loaded for sequencing and on-device target enrichment via Adaptive Sampling.

From extraction to library preparation and flow cell loading, sample preparation takes approximately 7.5–9.5 hours to complete.



**Sequencing:**  
performing high-coverage, on-device targeted sequencing

Find out more about the PromethION sequencing devices:  
[nanoporetech.com/promethion](https://nanoporetech.com/promethion)

The **PromethION 24** is a high-throughput device with powerful onboard compute, allowing you to sequence multiple samples of three with ease. This device features 24 flow cell positions and can keep up with real-time basecalling using the high accuracy (HAC) basecalling model, alongside reference genome alignment and Adaptive Sampling. For reduced throughput needs, the **PromethION 2 Integrated** features two flow cell positions.

The Hereditary Cancer Panel bundle includes a data pack that provides you with the necessary files for target enrichment via Adaptive Sampling. During the sequencing run set-up on **MinKNOW™** (the software that controls Oxford Nanopore sequencers), upload the files. These include a reference genome FASTA file and a target region BED file.

By sequencing three samples per flow cell, you can generate over 45 Gb of total data per flow cell. With this output, you can achieve >30x mean depth of coverage for all target genes, with a low-pass whole-genome sequencing (off-target) coverage of 3–5x<sup>5</sup>.

#### Panel specifications

Enrichment method	Adaptive Sampling
Genes	258
Reference genome	Hg38
Recommended DNA input	1 µg
Sample type	Whole blood, DNA
Coverage uniformity (fold-80)	1.2
Samples per PromethION Flow Cell	3
Total assay time (hands-on time)	<5 days (<2 hours)

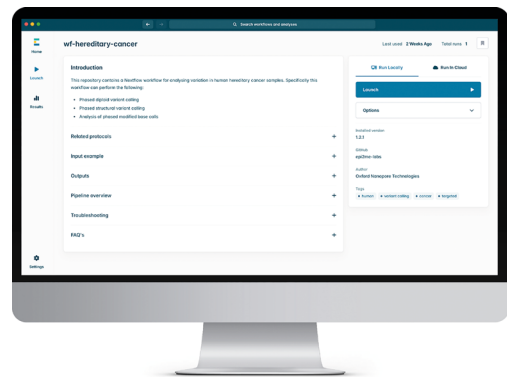
**Analysis:**  
investigating full-length hereditary cancer predisposition genes

Explore EPI2ME workflows:  
[nanoporetech.com/epi2me](https://nanoporetech.com/epi2me)

**EPI2ME™** is the data analysis platform from Oxford Nanopore, providing bioinformatic workflows for all levels of expertise. As part of the Hereditary Cancer Panel data pack, the **wf-hereditary-cancer** workflow is available for post-sequencing analysis.

This workflow is a simple point-and-click preconfigured pipeline that produces several interactive HTML reports, providing data quality metrics, coverage across target regions, and detected variants. Using this workflow, analyse a broad spectrum of variants, including SNVs, indels, SVs, and exon-level deletions, alongside epigenetic modifications.

Furthermore, additional files, such as VCF files, are generated and can be used for further downstream analysis, including tertiary variant annotation and haplotagged alignment.



View the end-to-end protocol: [nanoporetech.com/HCP-protocol](https://nanoporetech.com/HCP-protocol)

#### References:

1. Romero-Laorden, N. and Castro, E. *Curr. Probl. Cancer* 41(4):251–264 (2017). DOI: <https://doi.org/10.1016/j.cuprob.2017.02.009>
2. Tsaousis, G.N. et al. *BMC Cancer* 19:535 (2019). DOI: <https://doi.org/10.1186/s12885-019-5756-4>
3. Ceyhan-Birsoy, O. and Jayakumar, G. et al. *Genome Med.* 14(1):92 (2022). DOI: <https://doi.org/10.1186/s13073-022-01101-2>
4. Bilyalov, A., Nikolaev, S., and Shigapova, L. et al. *Biology* 11(10):1461 (2022). DOI: <https://doi.org/10.3390/biology11101461>
5. Oxford Nanopore Technologies. *Application note* (2025) <https://nanoporetech.com/resource-centre/application-note-comprehensive-genomic-and-epigenomic-profiling-with-the-oxford-nanopore-hereditary-cancer-panel> (2025) [Accessed 2 December 2025]



[www.nanoporetech.com](https://www.nanoporetech.com)

phone +44 (0)845 034 7900

email [support@nanoporetech.com](mailto:support@nanoporetech.com)

[oxford-nanopore-technologies](https://www.linkedin.com/company/oxford-nanopore-technologies)

@nanopore

@nanoporetech.com

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