HEREDITARY CANCER SOLUTION™ BY SOPHiA GENETICS

CE IVD

The Hereditary Cancer Solution (HCS) by SOPHiA GENETICS is a molecular diagnostic application that bundles the analytical power of SOPHiA™ AI with a capture-based target enrichment kit and full access to SOPHiA DDM® platform.

Knowledge-Driven Kit Design

SOPHiA™

The AI Democratizing Data-Driven Medicine

SOPHiA DDM®

SaaS Analytical Platform

The HCS panel covers the coding regions and splicing junctions (± 25bp) of 26 most clinically relevant genes (target region of 105 kb), associated with breast and ovarian cancer, HNPCC and intestinal polyposis syndromes. It guarantees high on-target reads percentage and coverage uniformity even in GC-rich regions, including the first exon.

Gene panel

ATM, APC, BARD1, BRCA1, BRCA2, BRIP1, CDH1, CHEK2, EPCAM, FAM175A, MLH1, MRE11A, MSH2, MSH6, MUTYH, NBN, PALB2, PIK3CA, PMS2, PMS2CL(1)*, PTEN, RAD50, RAD51C, RAD51D, STK11, TP53, XRCC2*

Recommendations

Starting material: 200 ng
Sample source: Blood
Samples per run: Depending on sequencing platform(2)

Sequencer	Flow Cell/ Sequencing Kit	Recommended samples per run (for 250x median coverage)
Illumina MiniSeq™	High Output Kit (2x150bp)	32
Illumina MiSeq®	v3 (2x300bp)	48
Illumina NextSeq® 500/550	Mid Output Kit (2x150bp)	Up to 96(3)

Wet lab

Day 1: Library Preparation
Day 2: Capture and Sequencing
Total hands-on time: 8 hours

SOPHiA analyses complex genomic NGS data by detecting, annotating and pre-classifying genomic variants to help clinicians better diagnose their patients.

- SNVs, Indels and CNVs are accurately detected in all genes of the panel
- Alu insertions are reliably recognized
- Pseudogene variants are efficiently differentiated from the ones in the *PMS2* gene(4)

SOPHiA leads to excellent clinical grade analytical performance(5):

	Observed	Lower 95% CI
Sensitivity	100%	99,20%
Specificity	100%	99,99%
Accuracy	100%	99,99%
Precision	99,86%	96,42%
Repeatability	99,98%	99,98%
Reproducibility	99,93%	99,93%
Average on-target rate	79,39%	
Coverage uniformity	99,72%	
Average percentage of target region depth > 200x	99,95%	

A total of 386 samples were processed on MiSeq® to obtain the above-mentioned metrics

Analysis time from FASTQ files: 4 hours(6)

The results are presented in SOPHiA DDM, the platform of choice for clinicians performing routine diagnostic testing. Thanks to its intuitive user interface and integrated features, variants visualization and interpretation are facilitated, while assuring protection of clinical genomic data.

Main features

Dedicated features in SOPHiA DDM reduce the complexity of determining the clinical significance of genomic variants.

- **Virtual Panels:** Restrict the interpretation to sub-panels of genes (e.g. focus on Lynch syndrome or breast cancer)
- **Variant Filter Builder:** Define and edit custom filters for efficient analysis
- **Interpretation Projects:** Create interpretation projects on datasets by restricting the analysis to a specific set of genes, associated with a defined disease or reflecting patient's consent

Access to the World's Largest Clinical Genomics Community

Through SOPHiA DDM, experts from hundreds of healthcare institutions can easily interpret the variants and flag them with the appropriate level of pathogenicity. This highly valuable information feeds the variant knowledge base and is anonymously and safely shared among the members of the community.

(1) The pseudogene *PMS2CL* is part of the analysis but not a gene responsible for disease
(2) Sequencing recommendations and specifications for other sequencing kits and instruments available upon request. The HCS is also compatible with Thermo Fisher Scientific platforms
(3) Maximum number of indices available
(4) Due to high gene conversion rates, a definite location in *PMS2* or *PMS2CL* cannot be assigned in homologous regions of exon 12-15
(5) Performance values have been calculated on SNVs and Indels only. The detection of CNVs, Alu repeats and pseudogene variants are not part of the CE-IVD claim
(6) Analysis time may vary depending on the number of samples multiplexed and server load


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sophiagenetics.com | info@sophiagenetics.com | @SOPHiAGENETICS