SOPHiA™

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SOPHiA HEREDITARY CANCER SOLUTION™ CE IVD

The molecular diagnostic application that bundles a capture-based target enrichment kit with the analytical power of SOPHiA™ AI and full access to the SOPHiA DDM® platform.

SMART KIT DESIGN

SOPHiA Hereditary Cancer Solution covers the coding regions and splicing junctions of the 26 most clinically relevant genes (target region of 105 kb), associated with breast and ovarian cancer, Lynch and intestinal polyposis syndromes. Probe design is optimized to guarantee high on-target rate and coverage uniformity even in GC-rich regions, including the first exon.

Gene panel

ABRAXAS1, ATM, APC, BARD1, BRCA1, BRCA2, BRIP1, CDH1, CHEK2, EPCAM, MLH1, MRE11, 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 / Ion Chip Kit	Recommended samples per run (for 250x median coverage depth)
Illumina MiSeq®*	v3 (2x300bp)	48
Illumina NextSeq® 500/550	Mid Output Kit (2x150bp)	Up to 96†
Ion Torrent™ Ion S5™ System	Ion 540™	Up to 48

*The CE-IVD mark only applies to Illumina MiSeq® using v3 chemistry
†Maximum number of indices available

Wet lab

Day 1: Library Preparation
Day 2: Capture and Sequencing
Library preparation time: 2 days

ANALYTICAL POWER

SOPHiA analyzes complex 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(3)

SOPHiA reaches clinical-grade analytical performance(4):

	Observed	Lower 95% CI
Sensitivity	100%	99.20%
CNV Sensitivity	99.28%*	
Specifity	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 % of target region with depth > 200x	99.95%	

A total of 159 samples were processed on MiSeq® to obtain the above-mentioned metrics
*CNV sensitivity was calculated on a total of 321 samples processed on Illumina MiSeq® instrument, with 139 confirmed CNVs.

Analysis time from FASTQ files: 4 hours(5)

UNIVERSAL PLATFORM

The results are presented in SOPHiA DDM, the platform of choice for clinicians performing routine diagnostic testing. Its intuitive user interface and advanced features facilitate the visualization and interpretation of genomic variants. Patients' data are kept safe by applying the highest industrial standards of encryption.

Main features

Dedicated features in SOPHiA DDM reduce the complexity of determining the significance of genomic variants and facilitate the interpretation process, thus reducing turnaround time.

- **Dual Variant Pre-Classification:** Improve assessment of variants pathogenicity with the pre-classification of both ACMG guidelines and SOPHiA's prediction
- **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 and dynamic analysis

Access to SOPHiA's Community

In SOPHiA DDM, experts from hundreds of healthcare institutions interpret the results and flag the pathogenicity level of variants according to their knowledge and experience. 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. Delivery time may vary according to the selected sequencing platform.
(3) Due to high gene conversion rates, a definite location in *PMS2* or *PMS2CL* cannot be assigned in homologous regions of *PMS2* exons 12-15.
(4) Performance values have been calculated based on SNVs and Indels in 159 samples processed on Illumina MiSeq®. The detection of CNVs, *Alu* repeats and pseudogene variants is not part of the CE-IVD claim. The CE-IVD mark only applies to Illumia MiSeq® using v3 chemistry.
(5) Analysis time may vary depending on the number of samples multiplexed and server load.