SOPHiA GENETICS™

Hereditary Cancer Solution

The genomic application that streamlines the analysis of complex mutational landscape associated with major hereditary cancer disorders by combining a capture-based target enrichment kit with the analytical performance* and advanced features of the SOPHiA DDM™ Platform.

Main Features

SOPHiA DDM™ Hereditary Cancer Solution covers the coding regions and splicing junctions of 26 genes (target region of 105 kb) associated with Hereditary Breast and Ovarian Cancer (HBOC), Lynch and various 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	Variants Called	Recommendations	Wet Lab
ABRAXAS1, APC, ATM, 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*	SNVs Indels CNVs *Alu* insertions *PMS2* vs *PMS2CL* variants[2] Boland inversion	**Starting material** 200 ng DNA **Sample type** Blood **Samples per run for >250x coverage depth / Sequencer (Flow Cell / Ion Chip Kit)[3]** 48 for Illumina MiSeq® v3 (2x300bp) Up to 96‡ for Illumina NextSeq® 500/550 Mid Output Kit (2x150bp) Up to 48 for Ion Torrent™ Ion S5™ System using Ion 540™ 96† on MGI DNBSEQ-G400, FCL, 1 lane of 4 (2x200)	**Day 1:** Library Preparation **Day 2:** Capture and Sequencing **Total library preparation time: 1.5 days**

‡ Maximum number of indices available.
† theoretical estimated maximum number of samples to be multiplexed, assuming 900 million reads per lane, and considering available kit size.

Analytical Performance*

The SOPHiA DDM™ Platform analyzes complex NGS data by detecting, annotating and pre-classifying multiple types of genomic variants in one unique experiment.

Analysis time from FASTQ: from 4 hours[4]

	Observed (%)	Lower 95% CI
Sensitivity	100	99.20
CNV Sensitivity	99.28	
Specificity	100	99.99
Accuracy	100	99.99
Precision	99.86	96.42
Repeatibility	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	

Performance values have been calculated based on SNVs and Indels in 159 samples processed on Illumina MiSeq®. CNV sensitivity was calculated on a total of 321 samples with 139 confirmed CNVs processed on Illumina MiSeq®.

One Simple Intuitive Platform: Beyond Analytics

Accelerated assessment and reporting of genomic variants

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 both ACMG scores and SOPHiA GENETICS™ machine learning –based predictions
- **Virtual Panel** - Restrict the interpretation to sub-panels of genes of interest using the HPO or OMIM® browser
- **Cascading Filters** - Apply custom filtering options for quicker screening of relevant variants and save strategies for future analyses

The platform can also provide access to Alamut™ Visual Plus, a full-genome browser that integrates numerous curated genomic and literature databases, guidelines, missense and slicing predictors, thus enabling a deeper variant exploration.
After the interpretation, you can generate a customizable variant report, including valuable information to support decision making.

Global support at every step

We offer local support anywhere in the world. Our dedicated bioinformaticians help save time and resources, ensuring fast resolution of workflow disruptions. In addition, our Set Up Program provides assistance with assay set up for fast and worry-free transition to routine testing.

Secure data storage

Access to the SOPHiA DDM™ Platform is restricted to registered users only. The Platform keeps data safe by applying the highest industrial standards of encryption in compliance with your local data security policies.

Access to the SOPHiA GENETICS™ community

In the SOPHiA DDM™ Platform, experts from hundreds of healthcare institutions interpret their 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. Due to high gene conversion rates, a definite location in *PMS2* or *PMS2CL* cannot be assigned in homologous regions of *PMS2* exons 12-15.
3. Sequencing recommendations and specifications for other sequencing kits and instruments available upon request. Delivery time may vary according to the selected sequencing platform.
4. Analysis time may vary depending on the number of samples multiplexed and server load.

***For Research Use Only. Not for Use in Diagnostic Procedures.**