SOPHiA GENETICS™

SOPHiA DDM™ Hereditary Cancer Solution v2.0

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

The SOPHiA DDM™ Hereditary Cancer Solution v2.0 (HCS v2.0) covers the coding regions and splicing junction of **83 genes** (target region of 285 kb) associated with Hereditary Breast and Ovarian Cancer (HBOC), Prostate and Abdominal Cancers, Endocrine and Neuroendocrine Cancers, Nervous System, Renal and Skin Cancers and all other major hereditary cancer syndromes. Probe design is optimized to guarantee high on-target rate and coverage uniformity even in GC-rich regions, including the first exon. It also includes Pengelly SNPs[1] for reliable sample tracking.

Gene Panel	Variants Called	Recommendations	Wet Lab
AIP, APC, ATM, AXIN2, BAP1, BARD1, BMPR1A, BRCA1, BRCA2, BRIP1, CDC73, CDH1, CDK4, CDKN1B, CDKN2A, CHEK2, CTNNA1, DICER1, DLST, EPCAM, FAM175A, FH, FLCN, GREM1, HOXB13, KIT, LZTR1, MAX, MDH2, MEN1, MET, MITF, MLH1, MLH3, MSH2, MSH3, MSH6, MUTYH, NBN, NF1, NF2, NTHL1, PALB2, PDGFRA, PIK3CA, PMS2, PMS2CL[2]*, POLD1, POLE, POT1, PRKAR1A, PRSS1, PTCH1, PTEN, RAD51C, RAD51D, RB1, RET, RNF43, SDHA, SDHAF2, SDHB, SDHC, SDHD, SEC23B, SLC25A11, SMAD4, SMARCA4, SMARCB1, SMARCE1, SPINK1, STK11, SUFU, TERC, TERT, TGFBR2, TMEM127, TP53, TSC1, TSC2, VHL, WRN, WT1*	SNVs Indels CNVs *Alu* insertions *PMS2* vs *PMS2CL* variants[3] Boland inversion	**Starting material** 50 ng DNA **Sample type** Blood **Samples per run for >250x coverage depth / Sequencer (Flow Cell / Ion Chip Kit)**[4] 16 for Illumina MiSeq® v3 (2x300bp*), 8-12 for v2 (2x150bp) 48 for Illumina NextSeq® 2000 P1, 192 for P2 72 for Illumina NextSeq® 500/550 mid-output, 192 for high-output 96** for 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

*The expected number of sequencing cycles is 200. **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[5]

	Observed
Sensitivity	100
CNV Sensitivity (1-2 exons)	98.00
Specificity	99.99
Accuracy	99.99
Precision	99.69
Repeatability	100
Reproducibility	99.43
Average on-target rate	84.57
Coverage uniformity	99.95
Average % of target region with depth >200x	99.79

Performance values have been calculated based on SNVs and Indels based on 6-108 samples processed on Illumina NextSeq®. CNV sensitivity was calculated on a total of 50 samples with confirmed CNVs processed on Illumina NextSeq®

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, the SOPHiA DDM™ MaxCare Program provides assistance with assay set up for a fast and worry-free transition to routine testing.

Secure and unlimited data storage

Access to the SOPHiA DDM™ Platform is restricted to registered users only. The Platform provides unlimited and unrestricted storage, while keeping data safe by applying the highest industrial standards of encryption in compliance with your local data security policies.

Access to the SOPHiA GENETICS™ Community

Through the SOPHiA DDM™ Platform, genomics experts from from hundred of healthcare institutions interpret their findings and flag the pathogenicity level of variants. This highly valuable information enriches the variant knowledge base and is safely shared among the members of the community, supporting their decision-making process for research purposes.

Product code: **BS0125ILLRGLY10**

1. Pengelly RJ, Gibson J, Andreoletti G, et al. Genome Med. 2013;5(9):89. doi: 10.1186/gm492
2. The pseudogene *PMS2CL* is part of the analysis but not a gene responsible for disease.
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. Sequencing recommendations and specifications for other sequencing kits and instruments available upon request. Delivery time may vary according to the selected sequencing platform.
5. Analysis time may vary depending on the number of samples multiplexed and server load.