

MSK-ACCESS[®] powered with SOPHiA DDM[™] is a decentralized version of the highly validated liquid biopsy assay developed and routinely used by Memorial Sloan Kettering Cancer Center (MSK)^{1,2}, involving the deep sequencing (~20,000x) of 147^a key cancer-associated genes. Powered by the advanced features of the SOPHiA DDM[™] Platform, the genomic application's sample-to-report workflow allows users to go from extracted cell-free DNA (cfDNA) to comprehensive report in an efficient timeframe (~5 days).

Main Features

- In-house hybrid capture workflow combined with cloud-based analytics, allowing users to retain control of samples and data.
- Matched tumor-normal analysis distinguishes somatic from germline and clonal hematopoiesis of indeterminate potential (CHIP) variants.
- Proprietary molecular barcoding approach, CUMIN[®], available exclusively on the SOPHiA DDM[™] Platform for increased sensitivity of variant detection.

Gene Panel	Variants Called	Recommendations	Wet Lab										
See next page for full gene list.	• SNVs and Indels in 147 genes^a • CNVs (whole gene amplifications and deletions) in 71 genes • Fusions (DNA-based via intronic targets) in 10 genes • TERT promoter • MET exon 14 skipping	Starting material >20 ng cfDNA, >50 ng white blood cell (WBC) gDNA Sample type Paired samples of cfDNA extracted from peripheral blood and WBC gDNA Recommended reads: Raw read depth: 100m fragments per tumor + normal pair Samples per run, theoretical multiplexing^b: <table><tr><td>Illumina NovaSeq™ 6000:</td><td>Illumina NovaSeq™ X:</td></tr><tr><td>SP flow cell: 8 (tumor + normal) pairs</td><td>1.5B: 16 (tumor + normal) pairs</td></tr><tr><td>S1 flow cell: 16 (tumor + normal) pairs</td><td>10B: 96 (tumor + normal) pairs</td></tr><tr><td>S2 flow cell: 40 (tumor + normal) pairs</td><td>25B: 256 (tumor + normal) pairs</td></tr><tr><td>S4 flow cell: 96 (tumor + normal) pairs</td><td></td></tr></table> Illumina NextSeq® 2000: P3 flow cell: 8 (tumor + normal) pairs, with 33% sequencing space left P4 flow cell: 16 (tumor + normal) pairs	Illumina NovaSeq™ 6000:	Illumina NovaSeq™ X:	SP flow cell: 8 (tumor + normal) pairs	1.5B: 16 (tumor + normal) pairs	S1 flow cell: 16 (tumor + normal) pairs	10B: 96 (tumor + normal) pairs	S2 flow cell: 40 (tumor + normal) pairs	25B: 256 (tumor + normal) pairs	S4 flow cell: 96 (tumor + normal) pairs		Day 1: Library preparation of cfDNA and WBC gDNA Day 2: Pooled tumor-normal capture and sequencing
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^aTERT promoter region included in total gene count.

^bIncorporation of the normal sample component requires only 10% of sequencing space.

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One Simple Intuitive Platform: Beyond Analytics

Accelerated assessment and reporting of genomic variants

The SOPHiA DDM[™] Platform helps users to immediately focus on relevant genomic alterations. Several features facilitate their interpretation process:

- Algorithm-supported variant pre-classification
- Fully customizable filters
- Comprehensive report

Reduced noise with a matched tumor-normal approach

MSK-ACCESS[®] powered with SOPHiA DDM[™] incorporates a paired tumor cfDNA and matched normal WBC DNA approach, thus enabling CHIP filtering and eliminating the risk of:

- Biological false positives at low allele frequencies.
- Removing true positives, if using external knowledge driven approaches.

Confident decision-making

The OncoPortal[™] Knowledge Base add-on module for the SOPHiA DDM[™] Platform matches tumor molecular profiles with clinical associations and available clinical trials, leveraging expertly curated evidence powered by Genomenon Cancer Knowledgebase. After interpretation, the flexible reporting tools enable users to prepare push-button, comprehensive reports that are customizable to their needs. In addition, access to MSK's precision oncology knowledge base, OncoKB[™], is provided via hyperlink.

Global support at every step

The SOPHiA DDM[™] MaxCare Program provides assistance with assay set up for fast and worryfree transition into routine analysis. In addition, we offer local support anywhere in the world. Our dedicated bioinformaticians help save time and resources, ensuring fast resolution of workflow disruptions.

Secure data storage

The SOPHiA DDM[™] Platform keeps data safe by applying the highest industrial standards of encryption in compliance with local data security policies.

Access to the SOPHiA GENETICS[™] Community

Through the SOPHiA DDM[™] Platform genomics experts from hundreds 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
BS2549ILLRSY14-32

Analytical Performance

The SOPHiA DDM[™] Platform analyzes complex NGS data by detecting, annotating and pre-classifying genomic alterations.

	Observed
SNV/Indel calling^c	
Sensitivity	99.4%
Specificity	99.999%
Fusion detection	
Concordance to confirmed status	100%
Reproducibility^d	R ² = 0.97
On-target rate	
cfDNA	89.5%
WBC DNA	89.0%
Coverage uniformity (molecule-based)	95.0%
Limit of detection	0.5% VAF

^cBased on end-to-end concordance analysis between MSK-ACCESS[®] powered with SOPHiA DDM[™] and centralized version of MSK-ACCESS[®] at MSK, using 48 cfDNA + matched WBC DNA samples; ^dCorrelation of variant allele fraction to reference method.

Gene list^a

AKT1 (3, 6, 7, 8, 9, 10, 11, 12), ALK (5, 9, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29), APC (full CDS), AR (full CDS), ARAF (7, 10, 11, 12, 13, 14, 15, 16), ARID1A (full CDS), ARID2 (8), ASXL1 (full CDS), ATM (full CDS), B2M (1), BAP1 (full CDS), BCL2 (2), BCOR (10), BRAF (11, 12, 13, 14, 15, 16, 17, 18), BRCA1 (full CDS), BRCA2 (full CDS), CARD11 (13), CFBF (2), CBL (9), CCND1 (5), CD79B (5), CDH1 (full CDS), CDK12 (full CDS), CDK4 (full CDS), CDKN2A (full CDS), CHEK2 (full CDS), CIC (5), CREBBP (26, 27, 30), CTCF (6), CTNNB1 (3, 7, 8), DICER1 (27), DIS3 (10), DNMT3A (full CDS), EGFR (3, 6, 7, 15, 18, 19, 20, 21, 22, 23, 24), EIF1AX (1, 2), EP300 (26, 27), ERBB2 (3, 6, 7, 8, 12, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 27), ERBB3 (3, 6, 7, 8, 9, 18, 19, 20, 21, 22, 23, 24), ERCC2 (full CDS), ESR1 (5, 6, 7, 8^b), EZH2 (16), FBXW7 (full CDS), FGFR1 (12, 13, 14, 15, 16, 17, 18, 19), FGFR2 (3, 5, 7, 8, 9, 11, 12, 13, 14, 15, 16, 17, 18), FGFR3 (7, 9, 11, 12, 13, 14, 15, 16, 17, 18), FGFR4 (13), FLT3 (14, 20), FOXA1 (2), FOXL2 (full CDS), FOXO1 (1), FOXF1 (14), FUBP1 (14), GATA3 (full CDS), GNA11 (5), GNAQ (5), GNAS (6, 8, 9), H3F3A (2), HIST1H3B (full CDS), HRAS (2, 3, 4), IDH1 (4, 5), IDH2 (4), IKZF1 (8), INPPL1 (2), JAK1 (19), JAK2 (14), KDM6A (full CDS), KEAP1 (full CDS), KIT (8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21), KNSTRN (1), KRAS (full CDS), MAP2K1 (2, 3, 4, 5, 6, 7, 8, 9, 10, 11), MAP2K2 (2, 3, 4, 5, 6, 7, 8, 9, 10, 11), MAPK1 (7), MAX (2, 4), MED12 (2, 26), MET (13, 14, 15, 16, 17, 18, 19, 20, 21), MLH1 (full CDS), MSH2 (full CDS), MSH3 (7), MSH6 (full CDS), MTOR (29, 30, 31, 39, 40, 43, 44, 46, 47, 48, 49, 50, 53, 56, 57), MYC (2), MYCN (2), MYD88 (5), MYOD1 (1), NF1 (full CDS), NFE2L2 (2), NOTCH1 (6, 8), NPM1 (11), NRAS (2, 3, 4), NTRK1 (13, 14, 15, 16, 17), NTRK2 (15, 16, 17, 18, 19), NTRK3 (15, 16, 17, 18, 19, 20), NUP93 (2), PAK5 (4), PALB2 (full CDS), PDGFRA (5, 6, 7, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21), PHF6 (5, 9), PIK3CA (2, 3, 5, 6, 8, 9, 10, 11, 12, 14, 19, 20, 21), PIK3CB (24), PIK3R1 (10, 11, 13, 14), PIK3R2 (10), PIM1 (1), PMS2 (full CDS), POLE (1, 9, 13), POT1 (6), PPM1D (full CDS), PPP2R1A (5, 6), PPP6C (7), PRKCI (15), PTCH1 (full CDS), PTEN (full CDS), PTPN11 (3, 13), RAC1 (2), RAD54L (10), RAF1 (7, 10, 11, 12, 13, 14, 15, 16, 17), RB1 (full CDS), RET (8, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19), RHOA (2, 3), RIT1 (5), ROS1 (36, 37, 38, 39, 40, 41, 42), RRAS2 (1, 3), RXRA (10), SETD2 (7), SF3B1 (14, 15, 18), SMAD3 (6), SMAD4 (full CDS), SMARCA4 (19, 25, 26), SMARCB1 (9), SOS1 (5), SPOP (4, 5), SRSF2 (1), STAT3 (20), STK11 (full CDS), STK19 (1), TCF7L2 (14), TET2 (full CDS), TGFBR1 (4, 9), TGFBR2 (8), TP53 (full CDS), TP63 (9, 14), TSC1 (full CDS), TSC2 (full CDS), U2AF1 (2, 6), VHL (full CDS), XPO1 (15)

Fusions

ALK, BRAF, EGFR, ETV6, FGFR2, FGFR3, MET, NTRK1, RET, ROS1

CNVs

AKT1, ALK, APC, AR, ARAF, ARID1A, ASXL1, ATM, BAP1, BRAF, BRCA1, BRCA2, CDH1, CDK12, CDK4, CDKN2A, CHEK2, CREBBP, DNMT3A, EGFR, EP300, ERBB2, ERBB3, ERCC2, ESR1, FBXW7, FGFR1, FGFR2, FGFR3, FOXA1, FOXL2, GATA3, KDM6A, KEAP1, KIT, KRAS, MAP2K1, MAP2K2, MET, MLH1, MSH2, MSH6, MTOR, MYC, MYCN, NF1, NTRK1, NTRK2, NTRK3, PAK5, PALB2, PDGFRA, PIK3CA, PIK3R1, PMS2, PPM1D, PTCH1, PTEN, RAF1, RB1, RET, ROS1, SF3B1, SMAD4, SMARCA4, STK11, TET2, TP53, TSC1, TSC2, VHL

MET exon 14 skipping

TERT promoter

^aCoverage details provided are based on SNV/indel calling, therefore, only CDS exons are included and not UTRs. ^bExons 5–8 based on reference sequence NM_000125.4. Exons 6–9 based on reference sequence NM_001122740.2. MSI regions – investigational use only, will not be available at first commercial launch.