SOPHiA GENETICS™

MSK-IMPACT® Flex powered with SOPHiA DDM™

The modular comprehensive genomic profiling (CGP) application that characterizes the complex mutational landscape of solid tumors, combining capture-based target enrichment technology and low-pass whole genome sequencing (lpWGS) with the advanced features of the SOPHiA DDM™ Platform.

Main Benefits

- Targets 533 genes from DNA and 140 genes from RNA for high-resolution profiling of all major variant classes and biomarkers, including TMB, MSI, HRD, and gene- and exon-level CNVs
- Leverages MSK-IMPACT® content for the DNA component, curated by clinical genomic experts at Memorial Sloan Kettering Cancer Center (MSK)
- Enhances efficiency through the modular design of SOPHiA DDM™ , enabling flexible combinations of DNA capture, RNA capture, and lpWGS (~1x) libraries at the sample level

Gene Panel

See page 2 for full gene list.

Variants Called

From DNA capture
- SNVs/Indels
- Gene-level and exon-level CNVs
- TMB
- MSI
- Fusions and exon skipping[a]

From DNA lpWGS
- HRD genomic integrity (GI)

From RNA capture
- Partner-agnostic fusions and exon skipping
- Gene expression

Recommendations

Starting material
50 ng DNA recommended
50 ng RNA recommended

Sample type
FFPE, fresh-frozen

Recommended reads
Total reads per sample
- DNA capture – 51 million
- RNA capture – 11 million
- DNA lpWGS – 20 million

Read length (BP)
2x150

Sequencers

- Illumina NextSeq® 550/550
- Illumina NextSeq® 1000/2000
- Illumina NovaSeq™ 6000
- Illumina NovaSeq™ X

For other sequencer types (e.g. Element and MGI), SOPHiA DDM™ MaxCare Program is recommended to verify performance.

Wet Lab (DNA only)

DNA library preparation
1 day

Hybridization[b]
Overnight

DNA capture and sequencing
0.5 days

Total workflow time
1.5 days

Wet Lab (DNA & RNA)

RNA reverse transcription
0.5 days

DNA & RNA library preparation
1 day

Hybridization[b]
Overnight

DNA & RNA capture and sequencing
0.5 days

Total workflow time
2 days

Product Codes

- BS0132ILLRSMY13 (DNA) – kit size 16, 32, 48, 96
- CS2517ILLRSRY16 (RNA) – kit size: 16, 32, 48, using Index plate A
- CS2517ILBRSRY16 (RNA) – kit size 96 using Index plate B
- DL0121ILLRSM (lpWGS –GIInger™) – dry lab

One Simple Intuitive Platform: Beyond Analytics

Accelerated assessment and reporting of genomic variants

The modular design enables tailored biomarker coverage at the sample level, allowing the efficient analysis of different data modalities within a single run.

All FASTQ files from the run can be uploaded to SOPHiA DDM™ together, after which the platform automatically performs the appropriate bioinformatic analyses and consolidates the results in a unified workspace.

Interpretation is streamlined through features such as algorithm-support variant pre-classification, pathogenicity prediction and fully customizable filters.

Confident decision-making

OncoPortal™ Knowledge Base is fully integrated into the SOPHiA DDM™ workflow and 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™ 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.

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

[a] Fusion results from DNA are available on SOPHiA DDM™ when activated. [b] Hybridization can also be performed during the day at a minimum of 4 hours.

CNV, copy number variant; HRD, homologous recombination deficiency; lpWGS, low-pass whole genome sequencing; MSI, microsatellite instability; TMB, tumor mutational burden.

Analytical Performance

Input	Biomarkers	PPA [%]	OPA [%]
DNA Capture			
	SNV/Indel[a]	100	-
	CNV (gene-level)[b]	91.8	-
	MSI[b]	100	97.9
	TMB[b]	90.0	95.8
	Gene fusion[c]	90.9	-
DNA lpWGS			
	HRD GI[d]	-	100
RNA Capture			
	Gene fusion and exon skipping[e]	100	100
	Gene expression[f]	100	-

Limit of detection at 95% (LOD95) for SNVs/Indels: <5% VAF (3.6% VAF)

Gene Content

DNA (533): *ABL1, ABRAXAS1, ACVR1, AGO1, AGO2, AKT1, AKT2, AKT3, ALB, ALK, ALOX12B, AMER1, ANKRD11, APC, APLNR, AR, ARAF, ARHGAP35, ARID1A, ARID1B, ARID2, ARID5B,* ***ASS1,*** *ASXL1, ASXL2, ATM, ATR, ATRX, ATXN7, AURKA, AURKB, AXIN1, AXIN2, AXL, B2M, BABAM1, BAP1, BARD1, BBC3, BCL10, BCL2, BCL2L1, BCL2L11, BCL6, BCOR,* ***BCORL1,*** *BIRC3, BLM, BMPR1A, BRAF, BRCA1, BRCA2, BRD4, BRIP1, BTK,* ***C11orf95,*** *CALR, CARD11, CARM1, CASP8, CBFB, CBL, CCND1, CCND2, CCND3, CCNE1, CCNQ, CD274, CD276,* ***CD58,*** *CD79A, CD79B, CDC42, CDC73, CDH1, CDK12, CDK4, CDK6, CDK8, CDKN1A, CDKN1B, CDKN2A, CDKN2B, CDKN2C, CEBPA, CENPA, CHEK1, CHEK2, CIC, CMTR2, COP1, CREBBP, CRKL, CRLF2, CSDE1, CSF1R, CSF3R, CTCF, CTLA4, CTNNB1, CTR9, CUL3, CXCR4, CXorf67, CYLD, CYP19A1, CYSLTR2, DAXX, DCUN1D1,* ***DDR1,*** *DDR2, DICER1, DIS3, DNAJB1, DNMT1, DNMT3A, DNMT3B, DOT1L,* ***DPYD,*** *DROSHA, DUSP4, E2F3, EED, EGFL7, EGFR, EIF1AX, EIF4A2, EIF4E, ELF3, ELOC, EP300, EPAS1, EPCAM, EPHA3, EPHA5, EPHA7, EPHB1, ERBB2, ERBB3, ERBB4, ERCC2, ERCC3, ERCC4, ERCC5, ERF, ERG, ERRFI1, ESR1, ETAA1, ETV1, ETV6, EZH1, EZH2, FANCA,* ***FANCB,*** *FANCC,* ***FANCD2, FANCE, FANCF, FANCG, FANCI, FANCL, FANCM, FAS,*** *FAT1, FBXW7, FGF19,* ***FGF23,*** *FGF3, FGF4, FGFR1, FGFR2, FGFR3, FGFR4, FH, FLCN, FLT1, FLT3, FLT4, FOXA1, FOXF1, FOXL2, FOXO1, FOXP1, FUBP1, FYN, GAB1, GAB2, GATA1, GATA2, GATA3,* ***GEN1,*** *GLI1, GNA11,* ***GNA13,*** *GNAQ, GNAS, GNB1, GPS2, GREM1, GRIN2A, GSK3B, H3F3A, H3F3B, H3F3C,* ***HDAC2,*** *HGF, HIST1H1C, HIST1H2BD, HIST1H3A, HIST1H3B, HIST1H3C, HIST1H3D, HIST1H3E, HIST1H3F, HIST1H3G, HIST1H3H, HIST1H3I, HIST1H3J, HIST2H3C, HIST2H3D, HIST3H3, HLA-A, HLA-B, HLA-C, HNF1A, HOXB13, HRAS, ICOSLG, ID3, IDH1, IDH2,* ***IDO2,*** *IFNGR1, IGF1, IGF1R, IGF2, IKBKE, IKZF1, IL10, IL7R, INHA, INHBA, INPP4A, INPP4B, INPPL1, INSR, IRF4, IRS1, IRS2, JAK1, JAK2, JAK3, JUN, KBTBD4, KDM5A, KDM5C, KDM6A, KDR, KEAP1, KIT, KLF4, KLF5, KMT2A, KMT2B, KMT2C, KMT2D, KMT5A, KNSTRN, KRAS, LATS1, LATS2,* ***LDB1,*** *LMO1, LYN, LZTR1, MAD2L2, MALT1, MAP2K1, MAP2K2, MAP2K4, MAP3K1, MAP3K13, MAP3K14, MAPK1, MAPK3, MAPKAP1, MAX, MCL1, MDC1, MDM2, MDM4, MED12, MEF2B, MEN1, MET, MGA, MITF, MLH1, MLLT1, MPL, MRE11, MSH2, MSH3, MSH6, MSI1, MSI2, MST1, MST1R, MTAP, MTOR, MUTYH, MYC, MYCL, MYCN, MYD88, MYOD1, NADK, NBN, NCOA3, NCOR1, NEGR1, NF1, NF2, NFE2L2, NFKBIA, NKX2-1, NKX3-1, NOTCH1, NOTCH2, NOTCH3, NOTCH4, NPM1, NRAS, NSD1, NSD2, NSD3, NTHL1, NTRK1, NTRK2, NTRK3, NUF2, NUP93, PAK1, PAK5, PALB2, PARP1, PAX5, PBRM1, PDCD1, PDCD1LG2, PDGFRA, PDGFRB, PDPK1, PGBD5, PGR, PHF6, PHOX2B, PIK3C2G, PIK3C3, PIK3CA, PIK3CB, PIK3CD, PIK3CG, PIK3R1, PIK3R2, PIK3R3, PIM1, PLCG2, PLK2, PMAIP1,* ***PML,*** *PMS1, PMS2, PNRC1, POLD1, POLE, POT1, PPARG, PPM1D, PPP2R1A,* ***PPP2R2A,*** *PPP4R2, PPP6C, PRDM1, PRDM14, PREX2, PRKAR1A, PRKCI, PRKD1, PRKN,* ***PRPF8,*** *PTCH1, PTEN, PTP4A1, PTPN11, PTPRD, PTPRS, PTPRT, RAB35, RAC1, RAC2, RAD21, RAD50, RAD51, RAD51B, RAD51C, RAD51D, RAD52, RAD54L, RAF1, RARA, RASA1, RB1, RBM10, RECQL, RECQL4, REL, REST, RET, RHEB, RHOA, RICTOR, RIT1, RNF43, ROS1, RPS6KA4, RPS6KB2, RPTOR, RRAGC, RRAS, RRAS2, RTEL1, RUNX1, RXRA, RYBP, SCG5, SDHA, SDHAF2, SDHB, SDHC, SDHD, SERPINB3, SERPINB4, SESN1, SESN2, SESN3, SETD2, SETDB1, SF3B1, SH2B3, SH2D1A, SHOC2, SHQ1, SLFN11, SLX4, SMAD2, SMAD3, SMAD4, SMARCA2, SMARCA4, SMARCB1, SMARCD1, SMARCE1, SMO, SMYD3, SOCS1, SOS1, SOX17, SOX2, SOX9, SPEN, SPOP, SPRED1, SPRTN, SRC, SRSF2, STAG2, STAT3, STAT5A, STAT5B,* ***STAT6,*** *STK11, STK19, STK40, SUFU, SUZ12, SYK, TAP1, TAP2, TBX3, TCF3, TCF7L2, TEK, TENT5C, TERT, TET1, TET2,* ***TFE3,*** *TGFBR1, TGFBR2, TMEM127, TMPRSS2, TNFAIP3, TNFRSF14, TOP1, TP53, TP53BP1, TP63, TRAF2, TRAF7, TRIP13, TSC1, TSC2, TSHR, U2AF1,* ***UGT1A1,*** *UPF1,* ***USH2A,*** *USP8, VEGFA, VHL, VTCN1, WT1, WWTR1, XIAP, XPO1, XRCC2, YAP1, YES1, ZFHX3, ZNRF3, ZRSR2*

Note: DNA genes in red are additional genes compared to the MSK-IMPACT® powered with SOPHiA DDM™ panel.

RNA (140): *ACVR2A, AKT1, AKT2, AKT3, ALK, ALPK1, ARHGA-P26, ARHGA-P6, AR, AXL, BCOR, BRAF, BRD3, BRD4, CAMTA1, CCNB3, CCND1, CHMP2A, CIC, CRTC1, CSF1, CSF1R, CTNNB1, DNAJB1, DICER1, EGF, EGFR, EPC1, ERBB2, ERBB4, ERG, ESR1, ESRRA, ETV1, ETV4, ETV5, ETV6, EWSR1, FGF1, FGFR1, FGFR2, FGFR3, FGR, FOSB, FOS, FOXO1, FOXO4, FOXR2, FUS, GLI1, GRB7, GREB1, HMGA2, HRAS,, IGF1R, INSR, JAK2, JAK3, JAZF1, KANSL1, KIT, KRAS, MAML2, MAP2K1, MAP3K8, MAST1, MAST2, MBTD1, MDM2, MEAF6, MET, MGEA5, MKL2, MN1, MSMB, MUSK, MYBL1, MYB, MYC, MYOD1, NCOA1, NCOA2, NCOA3, NFATC2, NFE2L2, NFIB, NOTCH1, NOTCH2, NR4A3, NRAS, NRG1, NTRK1, NTRK2, NTRK3, NUMBL, NUTM1, PAX3, PAX8, PDGFB, PDGFD, PDGFRA, PDGFRB, PHF1, PHKB, PIK3CA, PKN1, PLAG1, PPARG, PRDM10, PRKACA, PRKACB, PRKCA, PRKCB, PRKCD, PRKD1, PRKD2, PRKD3, RAD51B, RAF1, RELA, RET, ROS1, RSPO2, RSPO3, SS18L1, SS18, STAT6, TAF15, TCF12, TERT, TFE3, TFEB, TFG, THADA, TMPRSS2, USP6, VGLL2, WWTR1, YAP1, YWHAE*

CNV, copy number variant; GI, genomic integrity; HRD, homologous recombination deficiency; lpWGS, low-pass whole genome sequencing; MSI, microsatellite instability; OPA, overall percent agreement; PPA, positive percent agreement; TMB, tumor mutational burden.

[a] Based on analysis of 48 samples characterized with orthogonal method (735 confirmed SNVs, 208 confirmed Indels). [b] Based on analysis of 48 samples characterized with orthogonal method. [c] Based on analysis of 11 fusion events from matched DNA and RNA NGS data generated by four clinical laboratories in context of Early Access Program. [d] Based on analysis of 24 ovarian cancer samples characterized with gold standard orthogonal method. [e] Based on analysis of 19 unique RNA samples characterized with gold standard amplicon-based orthogonal method (99 confirmed events). [f] Based on analysis of 19 unique RNA samples (21 when including replicates) characterized with orthogonal targeted enrichment method.

Biomarkers

From DNA capture	
SNVs/Indels	**533 genes:** All genes of the panel
Gene-level (whole gene amplification and deletion)	**520 genes:** All genes of the panel **except** for *HIST2H3D, HIST2H3C, HIST1H3A, HIST1H3D, HIST1H3E, HIST1H3F, HIST1H3G, HIST1H3H, HIST1H3I, HIST1H3J, HLA-A, HLA-C, H3F3B*
Gene-level and exon-level CNV genes	**49 genes:** *APC, ARID1A, ATM, BAP1, BARD1, BRCA1, BRCA2, BRIP1, CDH1, CDK12, CHEK1, CHEK2, DICER1, EGFR, EPCAM, FANCA, FANCD2, FANCL, FH, FLCN, MET, MLH1, MRE11, MSH2, MSH6, NBN, NF1, NF2, PALB2, PMS2, PPP2R2A, PTCH1, PTEN, RAD51B, RAD51C, RAD51D, RAD54L, RB1, SDHA, SDHB, SDHC, SMARCA4, SMARCB1, STK11, SUFU, TP53, TSC1, TSC2, WT1*
DNA fusions[a]	**22 genes:** *ALK, BCL2L11(BIM), BRAF, CD74, DNAJB1, EGFR, ETV6, EWSR1, FGFR2, FGFR3, MET, NAB2, NTRK1, NTRK2, NUTM1, PAX8, RELA, RET, ROS1, TFE3, TMPRSS2, TP53*
Other biomarkers	MSI, TMB, TERT promoter
From DNA lpWGS	
Genomic integrity analysis for HRD	

[a] Fusion results from DNA are available on SOPHiA DDM™ when activated.

From RNA capture	
RNA fusions (partner-agnostic)	**135 genes:** *ACVR2A, AKT1, AKT2, AKT3, ALK*, ARHGA-P26, ARHGA-P6, AR, AXL, BCOR, BRAF*, BRD3, BRD4, CAMTA1, CCNB3, CCND1, CHMP2A, CIC, CRTC1, CSF1, CSF1R, CTNNB1, DNAJB1*, EGF, EGFR*, EPC1, ERBB2, ERBB4, ERG, ESR1, ESRRA, ETV1, ETV4, ETV5, ETV6*, EWSR1*, FGF1, FGFR1, FGFR2*, FGFR3*, FGR, FOSB, FOS, FOXO1, FOXO4, FUS, GLI1, GRB7, GREB1, HMGA2, IGF1R, INSR, JAK2, JAK3, JAZF1, KANSL1, KIT, KRAS, MAML2, MAP2K1, MAP3K8, MAST1, MAST2, MBTD1, MDM2, MEAF6, MET*, MGEA5, MKL2, MN1, MSMB, MUSK, MYBL1, MYB, MYC, MYOD1, NCOA1, NCOA2, NCOA3, NFATC2, NFE2L2, NFIB, NOTCH1, NOTCH2, NR4A3, NRG1, NTRK1*, NTRK2*, NTRK3, NUMBL, NUTM1*, PAX3, PAX8*, PDGFB, PDGFD, PDGFRA, PDGFRB, PHF1, PHKB, PIK3CA, PKN1, PLAG1, PPARG, PRDM10, PRKACA, PRKACB, PRKCA, PRKCB, PRKCD, PRKD1, PRKD2, PRKD3, RAD51B, RAF1, RELA*, RET*, ROS1*, RSPO2, RSPO3, SS18L1, SS18, STAT6, TAF15, TCF12, TERT, TFE3*, TFEB, TFG, THADA, TMPRSS2*, USP6, VGLL2, WWTR1, YAP1, YWHAE* ***Also in the scope of DNA-based fusion and exon skipping analysis.**
Exon skipping	**9 genes:** *ALK* (ex1–ex18; ex1–ex4), *AR* (ex3-ex4; *ARV7*, cryptic exon inclusion), *BRAF* (ex1–ex11; ex1–ex9; ex2–ex9; ex3–ex11; ex3–ex9), *EGFR* (ex1–ex8), *ERBB2* (ex15–ex17), *MET* (ex13–ex15; ex14–ex16), *NFE2L2* (ex1–ex3; ex1–ex4), *NOTCH1* (ex1–ex28; ex20–ex28; ex2–ex28; ex2–ex29), *PDGFRA* (ex7–ex10) Kinase domain duplications in *BRAF* (ex18–ex10), *EGFR* (ex25–ex18), *FGFR1* (ex18–ex10)
Gene expression	**56 genes:** *AKT1, AKT3, ALK, ALPK1, ARHGA-P26, BCOR, BRAF, CSF1, CTNNB1, DICER1, EGFR, ERBB2, ERG, ESR1, ETV1, ETV4, FGFR1, FGFR2, FGFR3, FUS, HMGA2, HRAS, JAK2, JAK3, KRAS, MAP2K1, MDM2, MET, MYBL1, MYOD1, NCOA1, NFE2L2, NFIB, NOTCH1, NRAS, NRG1, NTRK1, NTRK2, NTRK3, PDGFRA, PIK3CA, PKN1, PRKACA, PRKACB, PRKCD, RAD51B, RAF1, RET, ROS1, SS18L1, SS18, STAT6, TCF12, TFE3, THADA, YAP1*