Laboratory Bulletin

Tumor Type-Specific and Large Pan-Cancer Panels by Next Generation Sequencing

(Lung, Myeloma, Myeloid Neoplasms, GIST, Sarcoma, Melanoma, Colorectal and Neuro-oncologic Panels)

Effective Date: September 1, 2020

The Molecular Pathology Laboratory at Beaumont Health will offer Next Generation Sequencing that enables comprehensive genomic profiling of solid tumor and hematologic malignancies. This test is designed for sequencing both DNA and RNA for the detection of single nucleotide variants (SNV), insertion/deletion mutations (indels), gene copy number changes (CNV), and gene fusions. The assay can also assess the genomic biomarkers of microsatellite instability (MSI) and tumor mutational burden (TMB).

The test can be ordered as either the comprehensive 523 gene analysis, or one of eight tumor type-specific gene panels that analyze the most clinically relevant genes for that tumor type, as shown below. The pan-cancer biomarkers of MSI, TMB, and NTRK1/NTRK2/NTRK3 gene fusions are also included with all solid tumor panels. The individual panels will be available to order on the dates listed below.

1. **Lung Cancer NGS Panel (26 genes)** **Available 9/1/2020**

   AKT1, ALK, BRAF, DDR2, EGFR, ERBB2, FGFR1, FGFR3, HRAS, KRAS, MAP2K1, MET, MLH1 MSH2, MSH6, NRAS, NTRK1, NTRK2, NTRK3, PIK3CA, PMS2, PTEN, RET, ROS1, SMAD4, TP53

2. **Myeloma NGS Panel (27 genes)** **Available 10/1/2020**

   AKT2, AKT3, ATM, BIRC3, BRAF, CCND1, CDK4, CDKN1B, CDKN2A, CXCR4, EGFR, FGFR3, IDH1, IDH2, IRF4, IKZF1, JAK2, KDM6A, KRAS, MYC, MYD88, NRAS, PIK3CA, PIM1, RB1, STAT3, TP53

3. **Myeloid Neoplasms NGS Panel (42 genes)** **Available 10/1/2020**

   ABL1, ABL2, ASXL1, BCR, BCOR, BRAF, CALR, CBL, CEBPA, CSF3R, DNMT3A, ETV6, EZH2, FLT3, GATA1, GATA2, GNAS, HRAS, IDH1, IDH2, JAK2, KIT, KRAS, MLL, MYD88, MPL, NPM1, NRAS, PHF6, PTEN, PTPN11, RAD21, RUNX1, SETBP1, SF3B1, SRSF2, SMC3, STAG2, TET2, TP53, WT1, ZRSR2

4. **Gastrointestinal Stromal Tumor NGS Panel (8 genes)** **Available 11/1/2020**

   KIT, PDGFRA, SDHB, SDHC, SDHD, NTRK1, NTRK2, NTRK3

5. **Sarcoma NGS Panel (28 genes)** **Available 11/1/2020**

   ALK, APC, BRAF, CDK4, CTNNB1, ETV6, EWSR1, FOXO1, GLI1, IDH1, IDH2, KIT, MDM2, MYOD1, NAB2, NF1, NTRK1, NTRK2, NTRK3, PAX3, PAX7, PDGFRA, PDGFRB, SDHB, SDHC, SMARCB1, TFE3, WT1

6. **Melanoma NGS Panel (15 genes)** **Available 11/1/2020**

   BRAF, CTNNB1, GNA11, GNAQ, KIT, MAP2K1, NF1, NRAS, NTRK1, NTRK2, NTRK3, PDGFRA, PIK3CA, PTEN, TP53

7. **Colorectal Cancer NGS Panel (17 genes)** **Available 11/1/2020**

   ATK1, BRAF, HRAS, KRAS, MET, MLH1, MSH2, MSH6, NRAS, NTRK1, NTRK2, NTRK3, PIK3CA, PMS2, PTEN, SMAD4, TP53

8. **Neuro-oncologic NGS Panel (12 genes)** **Available 11/1/2020**

   ATRX, BRAF, CDKN2A, CDKN2B, CDKN2C, EGFR, HIST3H3, IDH1, IDH2, MYC, MYCN, MYCL1

9. **Comprehensive Cancer NGS Panel (523 genes)** **Available 12/1/2020**
   Listed on the last page of this bulletin

Synonyms:
TSO500, TruSight Oncology 500, next generation sequencing, NGS, lung panel, myeloma panel, myeloid panel, GIST panel, sarcoma panel, melanoma panel, colorectal panel, neuro panel.

Instructions:
This **test requires insurance preauthorization**. The laboratory will not perform sequencing without preauthorization.

Specimen Collection Criteria:

Bone Marrow:

1.0 mL bone marrow aspirate in a Lavender-top EDTA tube. (Minimum: 0.5 mL).

Solid Tumors:

Paraffin-embedded tissue block must be submitted with corresponding H&E slide. Unstained sections of 5-µm thickness mounted on glass slides can also be used (minimum 5 sections for large tissue and 10 sections for small tissue such as core biopsy). Tissue should be well fixed and well processed. Average tissue size 5.0 mm2.

- DNA will be assessed for quality. If it is deemed unacceptable, testing will be cancelled with client notification.
- The specimen must be accompanied by a completed requisition and must contain the patient name, date of birth, collection date, ordering physician, and source of specimen.

Specimen Preparation for Courier Transport:
Transport all bone marrow, tissue or slides, at room temperature (20-26°C or 68-78.8°F).

Rejection Criteria:

- Specimens collected in heparin (Green-top), clot tubes (Red-top), ACD anti-coagulant tubes, or SST tubes.
- Tissue decalcified with agents other than Mol Decal (EDTA)
- Fixatives other than 10% neutral buffered formalin.
- Improper labeling or inadequate information.
- Less than 10 percent tumor cellularity
- Poor quality and/or quantity of extracted genomic DNA.
- Frozen specimens.
- Unlabeled tubes or samples.

Testing will be cancelled on specimens meeting the above criteria with client notification. Under certain circumstances (i.e., lack of alternative specimens), testing may proceed with approval from the medical director or designee.

Performed:
Once or twice per week, dependent upon test volume. Results available in 10-15 business days.

Reference Range:
No variants detected or likely benign variants detected.

Test Methodology:
Tissue section slides are reviewed by a pathologist and relevant tumor is selected for analysis. RNA, DNA or both are isolated from the sample and quantified. Recovered nucleic acid extracts are prepared for sequencing with the Illumina TruSight Oncology 500 library preparation kit and sequenced on the Illumina NextSeq instrument with the Illumina TruSight Oncology 500 sequencing kit. Analysis is performed using PierianDx Clinical Genomics Workspace (CGW) software.

A personalized interpretive report is generated for each sample that lists the variants detected in each gene, classifies these based on a standardized classification scheme for somatic variants, and provides interpretative comments for each variant of known significance.

Interpretation:
Test results should be interpreted in the context of clinical findings, tumor sampling, and other laboratory data. If results obtained do not match other clinical or laboratory findings, please contact the laboratory director.

Test Code:

Panel Name	Soft code-5 character
Lung Cancer NGS Panel	MLUNG
Melanoma NGS Panel	MMEL
Colorectal Cancer NGS Panel	MCRC
Sarcoma NGS Panel	MSARC
Gastrointestinal Cancer NGS Panel	MGIST
Neuro-oncologic NGS Panel	MNEUR
Myeloma NGS Panel	MMYLM
Myeloid neoplasms NGS Panel	MMYLD
500 CANCER GENE PANEL NGS	M500G

CPT Code:

Panel Name	CPT codes
Lung Cancer NGS Panel	81445
Melanoma NGS Panel	81445
Colorectal Cancer NGS Panel	81445
Sarcoma NGS Panel	81445
Gastrointestinal Cancer NGS Panel	81445
Neuro-oncologic NGS Panel	81455
Myeloma NGS Panel	81450
Myeloid neoplasms NGS Panel	81450
500 CANCER GENE PANEL NGS	81455

Date submitted: August 12, 2020
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Genes included in the Comprehensive 523 gene panel

DNA content										
ABL1	BRD4	CUX1	FAM175A	GATA6	IGF1	MAP3K13	NOTCH4	POLE	RPTOR	TAF1
ABL2	BRIP1	CXCR4	FAM46C	GEN1	IGF1R	MAP3K14	NPM1	PPARG	RUNX1	TBX3
ACVR1	BTG1	CYLD	FANCA	GID4	IGF2	MAP3K4	NRAS	PPM1D	RUNX1T1	TCEB1
ACVR1B	BTK	DAXX	FANCC	GLI1	IKBKE	MAPK1	NRG1	PPP2R1A	RYBP	TCF3
AKT1	C11orf30	DCUN1D1	FANCD2	GNA11	IKZF1	MAPK3	NSD1	PPP2R2A	SDHA	TCF7L2
AKT2	CALR	DDR2	FANCE	GNA13	IL10	MAX	NTRK1	PPP6C	SDHAF2	TERC
AKT3	CARD11	DDX41	FANCF	GNAQ	IL7R	MCL1	NTRK2	PRDM1	SDHB	TERT
ALK	CASP8	DHX15	FANCG	GNAS	INHA	MDC1	NTRK3	PREX2	SDHC	TET1
ALOX12B	CBFB	DICER1	FANCI	GPR124	INHBA	MDM2	NUP93	PRKAR1A	SDHD	TET2
ANKRD11	CBL	DIS3	FANCL	GPS2	INPP4A	MDM4	NUTM1	PRKCI	SETBP1	TFE3
ANKRD26	CCND1	DNAJB1	FAS	GREM1	INPP4B	MED12	PAK1	PRKDC	SETD2	TFRC
APC	CCND2	DNMT1	FAT1	GRIN2A	INSR	MEF2B	PAK3	PRSS8	SF3B1	TGFBR1
AR	CCND3	DNMT3A	FBXW7	GRM3	IRF2	MEN1	PAK7	PTCH1	SH2B3	TGFBR2
ARAF	CCNE1	DNMT3B	FGF1	GSK3B	IRF4	MET	PALB2	PTEN	SH2D1A	TMEM127
ARFRP1	CD274	DOT1L	FGF10	H3F3A	IRS1	MGA	PARK2	PTPN11	SHQ1	TMPRSS2
ARID1A	CD276	E2F3	FGF14	H3F3B	IRS2	MITF	PARP1	PTPRD	SLIT2	TNFAIP3
ARID1B	CD74	EED	FGF19	H3F3C	JAK1	MLH1	PAX3	PTPRS	SLX4	TNFRSF14
ARID2	CD79A	EGFL7	FGF2	HGF	JAK2	MLL	PAX5	PTPRT	SMAD2	TOP1
ARID5B	CD79B	EGFR	FGF23	HIST1H1C	JAK3	MLLT3	PAX7	QKI	SMAD3	TOP2A
ASXL1	CDC73	EIF1AX	FGF3	HIST1H2BD	JUN	MPL	PAX8	RAB35	SMAD4	TP53
ASXL2	CDH1	EIF4A2	FGF4	HIST1H3A	KAT6A	MRE11A	PBRM1	RAC1	SMARCA4	TP63
ATM	CDK12	EIF4E	FGF5	HIST1H3B	KDM5A	MSH2	PDCD1	RAD21	SMARCB1	TRAF2
ATR	CDK4	EML4	FGF6	HIST1H3C	KDM5C	MSH3	PDCD1LG2	RAD50	SMARCD1	TRAF7
ATRX	CDK6	EP300	FGF7	HIST1H3D	KDM6A	MSH6	PDGFRA	RAD51	SMC1A	TSC1
AURKA	CDK8	EPCAM	FGF8	HIST1H3E	KDR	MST1	PDGFRB	RAD51B	SMC3	TSC2
AURKB	CDKN1A	EPHA3	FGF9	HIST1H3F	KEAP1	MST1R	PDK1	RAD51C	SMO	TSHR
AXIN1	CDKN1B	EPHA5	FGFR1	HIST1H3G	KEL	MTOR	PDPK1	RAD51D	SNCAIP	U2AF1
AXIN2	CDKN2A	EPHA7	FGFR2	HIST1H3H	KIF5B	MUTYH	PGR	RAD52	SOCS1	VEGFA
AXL	CDKN2B	EPHB1	FGFR3	HIST1H3I	KIT	MYB	PHF6	RAD54L	SOX10	VHL
B2M	CDKN2C	ERBB2	FGFR4	HIST1H3J	KLF4	MYC	PHOX2B	RAF1	SOX17	VTCN1
BAP1	CEBPA	ERBB3	FH	HIST2H3A	KLHL6	MYCL1	PIK3C2B	RANBP2	SOX2	WISP3
BARD1	CENPA	ERBB4	FLCN	HIST2H3C	KMT2B	MYCN	PIK3C2G	RARA	SOX9	WT1
BBC3	CHD2	ERCC1	FLI1	HIST2H3D	KMT2C	MYD88	PIK3C3	RASA1	SPEN	XIAP
BCL10	CHD4	ERCC2	FLT1	HIST3H3	KMT2D	MYOD1	PIK3CA	RB1	SPOP	XPO1
BCL2	CHEK1	ERCC3	FLT3	HLA-A	KRAS	NAB2	PIK3CB	RBM10	SPTA1	XRCC2
BCL2L1	CHEK2	ERCC4	FLT4	HLA-B	LAMP1	NBN	PIK3CD	RECQL4	SRC	YAP1
BCL2L11	CIC	ERCC5	FOXA1	HLA-C	LATS1	NCOA3	PIK3CG	REL	SRSF2	YES1
BCL2L2	CREBBP	ERG	FOXL2	HNF1A	LATS2	NCOR1	PIK3R1	RET	STAG1	ZBTB2
BCL6	CRKL	ERRFI1	FOXO1	HNRNPK	LMO1	NEGR1	PIK3R2	RFWD2	STAG2	ZBTB7A
BCOR	CRLF2	ESR1	FOXP1	HOXB13	LRP1B	NF1	PIK3R3	RHEB	STAT3	ZFHX3
BCORL1	CSF1R	ETS1	FRS2	HRAS	LYN	NF2	PIM1	RHOA	STAT4	ZNF217
BCR	CSF3R	ETV1	FUBP1	HSD3B1	LZTR1	NFE2L2	PLCG2	RICTOR	STAT5A	ZNF703
BIRC3	CSNK1A1	ETV4	FYN	HSP90AA1	MAGI2	NFKBIA	PLK2	RIT1	STAT5B	ZRSR2
BLM	CTCF	ETV5	GABRA6	ICOSLG	MALT1	NIKO2-1	PMAIP1	RNF43	STK11	
BMPR1A	CTLA4	ETV6	GATA1	ID3	MAP2K1	NIKO3-1	PMS1	ROS1	STK40	
BRAF	CTNNA1	EWSR1	GATA2	IDH1	MAP2K2	NOTCH1	PMS2	RPS6KA4	SUFU	
BRCA1	CTNNB1	EZH2	GATA3	IDH2	MAP2K4	NOTCH2	PNRC1	RPS6KB1	SUZ12	
BRCA2	CUL3	FAM123B	GATA4	IFNGR1	MAP3K1	NOTCH3	POLD1	RPS6KB2	SYK	
RNA content*										
ABL1	BCL2	CSF1R	ESR1	EWSR1	FLI1	KIF5B	MSH2	NRG1	PAX7	RAF1
AKT3	BRAF	EGFR	ETS1	FGFR1	FLT1	KIT	MYC	NTRK1	PDGFRA	RET
ALK	BRCA1	EML4	ETV1	FGFR2	FLT3	MET	NOTCH1	NTRK2	PDGFRB	ROS1
AR	BRCA2	ERBB2	ETV4	FGFR3	JAK2	MLL	NOTCH2	NTRK3	PIK3CA	RPS6KB1
AXL	CDK4	ERG	ETV5	FGFR4	KDR	MLLT3	NOTCH3	PAX3	PPARG	TMPRSS2

* The products to evaluate DNA and RNA variants consist of the TruSight Oncology 500 DNA panel and the TruSight Tumor 170 RNA panel.