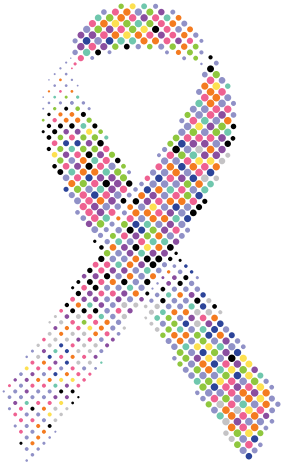
MEDGENOME | Prima Cancer Genetics

CAP ACCREDITED
COLLEGE of AMERICAN PATHOLOGISTS

TumorTrack Advance

For Precision Oncology



Comprehensive Genomic Profiling

Single Assay, Multiple Biomarkers | Tumor Agnostic | Tissue Testing

350+ Clinically Relevant Cancer Related Genes

Benefits

- Detects multiple biomarkers in a single assay
- Identify actionable/ potentially actionable biomarkers
- Saves time and precious sample by consolidated testing

Improved Patient Outcomes

TumorTrack Advance Test

TumorTrack Advance is a next generation sequencing (NGS) assay consisting of DNA and RNA based testing which detects single nucleotide variants (SNVs),small insertion-deletion mutations (InDels), copy number variants (CNVs), fusions, tumor mutation burden (TMB), microsatellite instability (MSI) and PD-L1 expression in multiple solid tumors.

Coverage

Coverage of Biomarkers

Breast

ATK1
AR
BRCA1
BRCA2
ERBB2
ESR1
FGFR1
FGFR2
PIK3CA
PTEN

Ovarian

BRCA1
BRCA2
KRAS
PDGFRA
FOXL2
TP53
ATM
BARD1
BRIP1
CDK12
CHEK1
CHEK2
FANCL
PALB2
PPP2R2A
RAD51B
RAD51C
RAD51D
RAD54L

Endometrial

POLE
MLH1
MSH2
PMS2
MSH6
TP53
ERBB2
ESR1

Colon

AKT1
BRAF
HRAS
KRAS
MET
MLH1
SMAD4
MSH2
MSH6
NRAS
PIK3CA
PMS2
PTEN
Her2 Amplification

Pancreatic

ALK
BRAF
BRCA1
BRCA2
ERBB2
KRAS
NRG1
PALB2
ROS1

Prostate

ATM
BRCA1
BRCA2
MLH1
MSH2
PMS2
MSH6
AR
BARD1
BRIP1
CDK12
CHEK1
CHEK2
FANCL
PALB2
PPP2R2A
RAD51B
RAD51C
RAD51D
RAD54L

Lung

AKT1
ALK
BRAF
DDR2
EGFR
ERBB2
FGFR1
FGFR2
FGFR3
KRAS
MAP2K1
MET
NRAS
PIK3CA
PTEN
RET
TP53
Her2 Amplification

Pan-Cancer

NTRK1
NTRK2
NTRK3

*Performed by IHC (SP263 /SP142/22c3)

Only major Tumor types /genes are mentioned here

IHC - Immunohistochemistry

Features

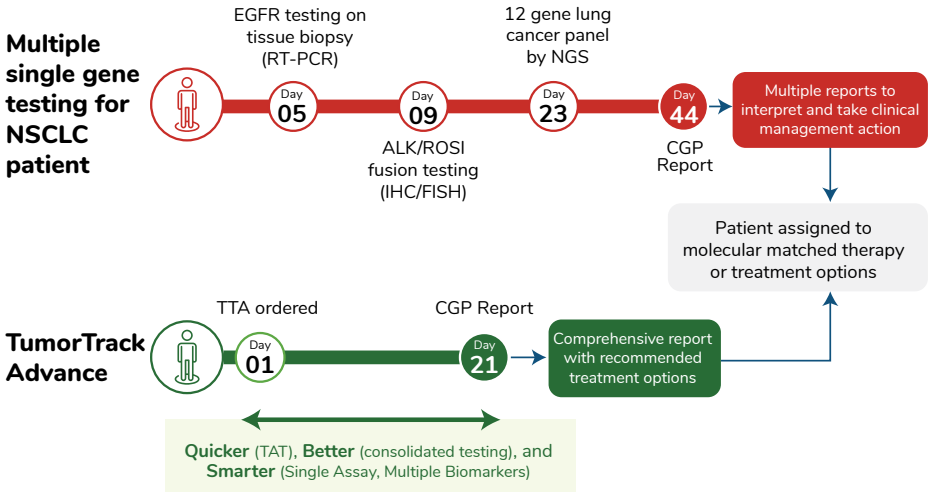
Single holistic test for the diagnosis, prognosis and to determine treatment options (Targeted Therapy & Immunotherapy)

- All genes recommended by guidelines (FDA, NCCN, ASCO, ESMO) across tumor types are covered
- Comprehensive coverage of complete coding regions of all the genes and intron/exon boundaries
- Well validated as per CAP guidelines; >98% sensitivity and specificity with 100% accuracy and precision using orthogonal assays/reference standards
- CAP accredited test; Performed 100% in biannual proficiency testing conducted by CAP
- High throughput Illumina's sophisticated NGS sequencing platforms
- Fusions and splice variants assessed via RNA analysis; sensitivity more than DNA analysis
- Global standards for the best laboratory practices followed
- Analysis and reporting as per ACMG/AMP/ASCO/CAP guidelines; CE-IVD certified mutation database for variant interpretation and reporting

TumorTrack Advance: Bioinformatics & Reporting Expertise

- Qualified team of bioinformatics engineers.
- Stringent quality checks are performed for each reported variant.
- Bioinformatics data analysis pipeline validated according to CAP guidelines.
- Expert genome analysts team for variant prioritization, interpretation and reporting.

Patient Journey with Multiple Single Gene Testing Vs CGP



TumorTrack Advance - CGP (Comprehensive Genomic Profiling)

NSCLC - Non-small cell lung cancer

Quick Facts

01 Importance of multi-gene molecular testing

Cancer is heterogeneous disease may develop by interplay of alterations in multiple genes which play an important role in cell growth, differentiation and cell death. Sequencing of single genes does not provide complete knowledge of pathways that are affected and often, relevant information is not available. The prognosis & treatment decisions may depend on multiple gene mutations.

02 Benefits of comprehensive genomic profiling

- ✓ To identify potential targeted therapies in a newly diagnosed cancer patient
- ✓ To determine the diagnosis and prognosis of the disease
- ✓ To detect drug resistance and plan on change of treatment regimen
- ✓ Determining the next course of action in patients that have progressed on first / second line treatment
- ✓ Designing treatment strategies in patients with unknown primary cancer
- ✓ Selection of patients for clinical trials

03 Coverage of actionable biomarkers

1. All genes recommended by guidelines (FDA, NCCN, ASCO, ASMO) across tumor types are covered
2. SNVs, InDels, CNVs, Fusions, TMB, MSI and PD-L1 by IHC.
3. All homologous recombination repair (HRR) pathway genes including BRCA1 & BRCA2 are covered

Actionable/potentially actionable variants identified in cancer patient samples from published data

93.5%

Single center, prospective study, 339 patients. Refractory cancers, (Wheler et al, 2016)

71%

6832 NSCLC patients

(Suh et al, 2016)

43%

221 patients with multiple cancer, multi-center study (Mathew et al, 2022) **MedGenome contributed data**

31.7%

7494 sarcoma patients; 44 different histologies (Gounder et al, 2022)

90%

Retrospective study with 96 patients across multiple tumor types (Suh et al, 2016)

NSCLC - Non-small cell lung cancer

Test Details

Test Name	Test Code	Sample Type	TAT
TumorTrack Advance (SNVs, InDels, CNVs, Fusions, TMB, MSI and PD-L1)	MGM1785 + PD-L1 Expression by IHC*	 FFPE Tissue Block >10% Tumor content - Histopathology Report	**21** Working days
TumorTrack Plus (SNVs, InDels, CNVs, Fusions, TMB and MSI)	MGM1785		
TumorTrack (SNVs, InDels, CNVs and Fusions)	MGM1879		
TumorTrack + MSI	MGM1784		
TumorTrack +TMB	MGM1558		
TumorTrack without Fusions	MGM196		
Tumour Mutation Burden (TMB) Analysis	MGM1556		14 working days

*SP263 /SP142/22c3

Assay Specifications

Cancer Type	All Solid Tumor Types
Specimen Types	FFPE Tissue Block/Cytology Cell Block, Tissue in RNA later*
FFPE block requirement*	Cross-sectional tumor area of 25mm² containing at least 40 µm of tumor tissue
Tumor Purity Minimum	>10% (as determined by Molecular Pathologist)
Limit of detection	• 5% VAF for SNV and InDels • >10 Spanning Reads for Fusions • >2.5-fold Change for CNV
Average Depth of sequencing	>250X
Analytical Sensitivity	99.15% (SNVs/InDels); 98% Fusions; ≥85-90% (CNVs)
Analytical Specificity	>99.9%

*Tumor Cellularity can not be determined for tissue in RNA later samples
VAF : Variant Allele Frequency

Case Studies

Non Small Cell Lung Cancer (NSCLC)

Clinical Scenario: A 43 year old female with Metastatic NSCLC (Adenocarcinoma)

Purpose of testing:
To detect actionable mutations *EGFR, ALK, ROS1, RET, MET, NTRK and other* genes along with immunotherapy options

Genomic Testing:
TumorTrack test on FFPE Tissue block with >10% tumor content

Findings & Implications:

1. **EGFR (exon20 insertion):** Resistance to EGFR TKI inhibitors
2. **BRCA1** variant found: Clinical trial for PARP inhibitors available

Melanoma

Clinical Scenario: Metastatic malignant melanoma

Purpose of testing:
To detect actionable mutation in *CKIT, PDGFRA, BRAF* and other genes along with immunotherapy options

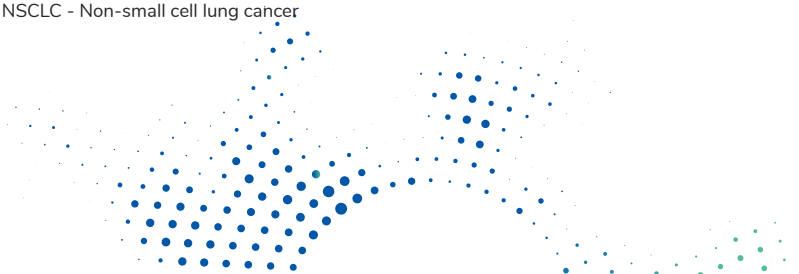
Genomic Testing:
TumorTrack test on FFPE Tissue block with >10% tumor content

Findings & Implications:

- **EWSR1-ATF1** fusion detected.
- This fusion is reported as a atypical fusion in melanoma patients. EWSR1-ATF1 is known as a driver fusion in clear cell sarcoma patients (malignant melanoma of soft tissues)

Hence, it is unique diagnostic finding. The identification of novel molecular markers may be useful for the improved diagnosis of melanoma, as well as for potentially indicating the prognostic and predictive value of various types of therapy.

NSCLC - Non-small cell lung cancer



Comparison Table

Parameters	TumorTrack Advance	Other Labs	Foundation One
Total number of genes covered	392 genes	<200 genes	324 genes
Base substitutions, indels and CNVs	231 genes	>200 genes	315 genes
Fusions	161 genes (RNA seq)	>50 genes	28 genes (DNA seq)
Tumor Mutation Burden (TMB)	1.1Mb	✗	1.5 Mb panel
Microsatellite Instability (MSI)	Yes (PCR or Fragment analysis)	✗	✓
Complete Gene coverage	✓	Mostly only hotspots are covered	✓
Homologous Recombination Repair (HRR) genes covered	✓	✗	✓
Sequencing Platform	Illumina NGS	Other than Illumina	Illumina NGS
Unique molecular identifier (UMI) based technology	✓	✗	✓
Depth of sequencing	>250x	NA	NA
Validation	Well-validated according to CAP guidelines	NA	FDA Approved
Variant Interpretation/ Reporting	ACMG/AMP/ASCO/ CAP Guidelines	NA	ACMG/AMP/ASCO/ CAP Guidelines
Accreditation	CAP	NA	FDA
PD-L1 expression by IHC	SP263, SP142 and 22c3 (Automated platform)	✗	✓
Genomic expert consultation	✓	✗	✓
Turnaround time	21 working days	21 to 24 working days	30 working days
Follow up MRD by NGS option	✓	✗	✓

MRD - Minimal Residual Disease
IHC - Immunohistochemistry

Gene List

DNA (SNVs, InDels and CNVs)								
ABRAXAS1	CARD11	DDR2	FGF14	HNF1A	MET	NRAS	**RAD51D**	STAT6
AKT1	CCND1	DDX3X	FGF19	HRAS	MFHAS1	NRG1	**RAD54L**	STK11
AKT2	CCND2	DNMT3A	FGF2	ID3	MLH1	NTRK1	RAF1	SUFU
AKT3	CCND3	EGFR	FGF23	IDH1	MLLT3	NTRK3	RB1	TCF3
ALK	CCNE1	EIF1AX	FGF3	IDH2	MN1	**PALB2**	RET	TERT
APC	CD28	EP300	FGF4	INPP4B	MPL	PDGFRA	RHOA	TET2
AR	CD58	ERBB2	FGF5	IRF4	MRE11	PDGFRB	RICTOR	TFRC
ARID1A	CD79A	ERBB3	FGF6	ITPKB	MSH2	PIK3CA	ROS1	TG
ARID1B	CD79B	ERBB4	FGF7	JAK2	MSH3	PIK3CB	RPS6KB1	TGFBR2
ARID2	CDH1	ERCC1	FGF8	JAK3	MSH6	PIK3CD	SDHA	TNFAIP3
ATM	**CDK12**	ERCC2	FGF9	KDM6A	MTOR	PIK3CG	SDHAF2	TNFRSF14
ATR	CDK4	ERCC3	FGFR1	KDR	MUTYH	PIK3R1	SDHB	TP53
ATRX	CDK6	ERCC4	FGFR2	KEAP1	MYB	PIM1	SDHC	TRAF3
B2M	CDKN2A	ERCC5	FGFR3	KIT	MYBL1	PMS2	SDHD	TRAF7
BAP1	CDKN2B	ERG	FGFR4	KLF4	MYC	POLD1	SF3B1	TSC1
BARD1	CEBPA	ESR1	FLT1	KMT2A	MYCL	POLE	SLX4	TSC2
BCL2	CHD8	EZH2	FLT3	KMT2C	MYCN	PPARG	SMAD4	TSHR
BCL6	**CHEK1**	FANCA	FOXL2	KMT2D	MYD88	**PPP2R2A**	SMARCA4	VHL
BCORL1	**CHEK2**	FANCB	FOXO1	KRAS	NBN	PRDM1	SMARCB1	XPC
BIRC3	CIC	FANCC	GEN1	LAMP1	NF1	PTCH1	SMARCE1	XPO1
BLM	CIITA	FANCE	GNA11	MAP2K1	NF2	PTEN	SMO	XRCC1
BRAF	CREBBP	FANCI	GNA13	MAP2K2	NFE2	PTPN11	SOCS1	XRCC2
BRCA1	CSF1R	**FANCL**	GNAQ	MCL1	NOTCH1	RAD50	SOX11	ZAP70
BRCA2	CSF3R	FBXW7	GNAS	MDM2	NOTCH2	RAD51	SRC	
BRIP1	CTNNB1	FGF1	H3-3A	MDM4	NOTCH3	**RAD51B**	STAT3	
BTK	CXCR4	FGF10	H3C2	MEF2B	NPM1	**RAD51C**	STAT5B	

RNA (Fusions)								
ABL1	CSF1	FGFR1	HOXA11	LCK	NCOA1	PHF1	ROS1	TFEB
AKT3	CSF1R	FGFR2	HOXA13	LMO1	NCOA2	PI3K	RPS5KB1	TFG
ALK	CTLA4	FGFR3	HOXA2	LMO2	NCOA3	PICALM	RPS6KB1	THADA
AR	DNAJB1	FGFR4	HOXA3	LYL1	NOTCH1	PIK3CA	RSPO2	TLX1
ASPL	DUSP22	FLI1	HOXA4	MAML2	NOTCH2	PIK3R2	RSPO3	TLX3
AXL	EGFR	FLT1	HOXA5	MDM2	NOTCH3	PLAG1	SAS	TMPRSS2
BCL2	EML4	FLT3	HOXA6	MEAF6	NRG1	PLCG1	SLC5A5	TP53
BCL6	EPC1	FLT4	HOXA7	MEN1	NTRK1	PPARG	SS18	TP63
BCOR	ERBB2	FOS	HOXA9	MET	NTRK2	PRKACA	SSX1	TPM3
BRAF	ERG	FOSB	INI1	MGEA5	NTRK3	PRKCA	SSX2	UACA
BRCA1	ESR1	FUS	IRF4	MKL2	NUTM1	PRKCB	SUZ12	USP6
BRCA2	ETS1	GLI	ITK	MLLT3	OGA	PRKCD	SYN2	VGLL2
CCND1	ETV1	GNA14	JAK2	MSH2	PAX3	PTH	TAF15	VGLL3
CCND2	ETV4	GRB7	JAZF1	MYB	PAX7	PTPBR	TAF2N	WWTR1
CDK4	ETV5	HEY1	KDR	MYBL1	PAX8	RAF1	TCF12	YAP1
CDKN2A	ETV6	HMGA2	KIF5B	MYC	PDGFB	RELA	TCF3	YWHAE
CLIP1	EWSR1	HOXA1	KIT	MYOD1	PDGFRA	RET	TCL1A	ZC3H7B
COL1A1	FARSB	HOXA10	KMT2A	NAB2	PDGFRB	RNF213	TFE3	

*All fusion partners for the genes covered in RNA Panel can be detected in this assay
*All 15 HRR genes covered (Bold)
*All genes with FDA approved drugs and/or strong clinical evidence are covered across tumor types (color shaded)

Talk to the Experts

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