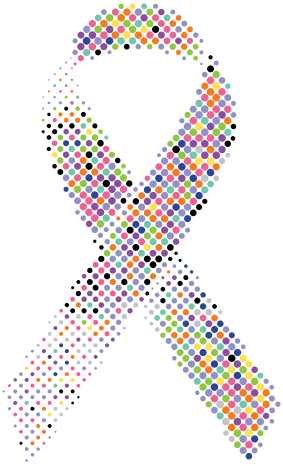
MEDGENOME | Prima Cancer Genetics

CAP ACCREDITED
COLLEGE of AMERICAN PATHOLOGISTS

TumorTrack Advance

For Precision Oncology



Comprehensive Genomic Profiling

Single Assay, Multiple Biomarkers | Tumor Agnostic | Tissue Testing

500+ 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), 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, PD-L1, PGR

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, PD-L1*, Her2 Amplification

Pan-Cancer

NTRK1, NTRK2, NTRK3, TMB, MSI, PD-L1*

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

IHC - Immunohistochemistry

Only major Tumor types /genes are mentioned here

Features

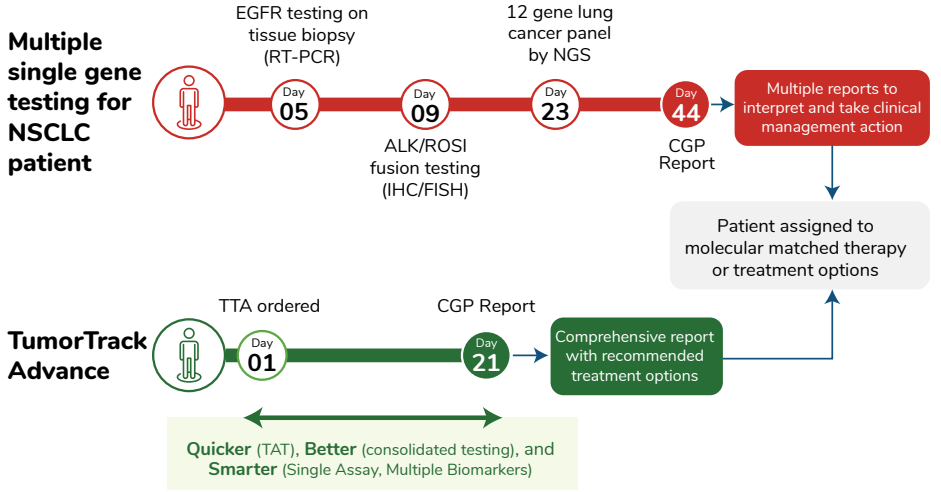
Single holistic test for the diagnosis, prognosis and to determine treatment options (Targeted Therapy & Immunotherapy)

- 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)
From India - 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	MGM1556		
TumorTrack without Fusions	MGM2559		

*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	583 genes	<200 genes	324 genes
Base substitutions, indels and CNVs	231 genes	>200 genes	315 genes
Fusions	91 genes	>50 genes	28 genes
Tumor Mutation Burden (TMB)	485 genes spanning 1.65Mb	✗	324 genes spanning 1.5 Mb
Microsatellite Instability (MSI)	Yes (NGS 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	AKT1	AKT2	AKT3	ALK	APC	AR	ARID1A	ARID1B
ARID2	ATM	ATR	ATRX	B2M	BAP1	BARD1	BCL2	BCL6
BCORL1	BIRC3	BLM	BRAF	BRCA1	BRCA2	BRIP1	BTK	CARD11
CCND1	CCND2	CCND3	CCNE1	CD28	CD58	CD79A	CD79B	CDH1
CDK12	CDK4	CDK6	CDKN2A	CDKN2B	CEBPA	CHD8	CHEK1	CHEK2
CIC	CIITA	CREBBP	CSF1R	CSF3R	CTNNB1	CXCR4	DDR2	DDX3X
DNMT3A	EGFR	EIF1AX	EP300	ERBB2	ERBB3	ERBB4	ERCC1	ERCC2
ERCC3	ERCC4	ERCC5	ERG	ESR1	EZH2	FANCA	FANCB	FANCC
FANCE	FANCI	FANCL	FBXW7	FGF1	FGF10	FGF14	FGF19	FGF2
FGF23	FGF3	FGF4	FGF5	FGF6	FGF7	FGF8	FGF9	FGFR1
FGFR2	FGFR3	FGFR4	FLT1	FLT3	FOXL2	FOXO1	GEN1	GNA11
GNA13	GNAQ	GNAS	H3-3A	H3C2	HNF1A	HRAS	ID3	IDH1
IDH2	INPP4B	IRF4	ITPKB	JAK2	JAK3	KDM6A	KDR	KEAP1
KIT	KLF4	KMT2A	KMT2C	KMT2D	KRAS	LAMP1	MAP2K1	MAP2K2
MCL1	MDM2	MDM4	MEF2B	MET	MFHAS1	MLH1	MLLT3	MN1
MPL	MRE11	MSH2	MSH3	MSH6	MTOR	MUTYH	MYB	MYBL1
MYC	MYCL	MYCN	MYD88	NBN	NF1	NF2	NFE2	NOTCH1
NOTCH2	NOTCH3	NPM1	NRAS	NRG1	NTRK1	NTRK3	PALB2	PDGFRA
PDGFRB	PIK3CA	PIK3CB	PIK3CD	PIK3CG	PIK3R1	PIM1	PMS2	POLD1
POLE	PPARG	PPP2R2A	PRDM1	PTCH1	PTEN	PTPN11	RAD50	RAD51
RAD51B	RAD51C	RAD51D	RAD54L	RAF1	RB1	RET	RHOA	RICTOR
ROS1	RPS6KB1	SDHA	SDHAF2	SDHB	SDHC	SDHD	SF3B1	SLX4
SMAD4	SMARCA4	SMARCB1	SMARCE1	SMO	SOCS1	SOX11	SRC	STAT3
STAT5B	STAT6	STK11	SUFU	TCF3	TERT	TET2	TFRC	TG
TGFBR2	TNFAIP3	TNFRSF14	TP53	TRAF3	TRAF7	TSC1	TSC2	TSHR
VHL	XPC	XPO1	XRCC1	XRCC2	ZAP70			

RNA (Fusions)								
ABL1	AKT3	ALK	AR	AXL	BCL2	BCL6	BRAF	BRCA1
BRCA2	CCND1	CCND2	CDK4	CDKN2A	CSF1R	CTLA4	DUSP22	EGFR
EML4	ERBB2	ERG	ESR1	ETS1	ETV1	ETV4	ETV5	EWSR1
FGFR1	FGFR2	FGFR3	FGFR4	FLI1	FLT1	FLT3	FUS	HOXA1
HOXA10	HOXA11	HOXA13	HOXA2	HOXA3	HOXA4	HOXA5	HOXA6	HOXA7
HOXA9	IRF4	ITK	JAK2	KDR	KIF5B	KIT	KMT2A	LCK
LMO1	LMO2	LYL1	MDM2	MET	MLLT3	MSH2	MYB	MYBL1
MYC	NOTCH1	NOTCH2	NOTCH3	NRG1	NTRK1	NTRK2	NTRK3	PAX3
PAX7	PDGFRA	PDGFRB	PIK3CA	PPARG	RAF1	RELA	RET	ROS1
RPS5KB1	RPS6KB1	SS18	TCF3	TCL1A	TLX1	TLX3	TMPRSS2	TP53
TP63								

*All fusion partners for the genes covered in RNA Panel can be detected in this assay
*All 15 HRR genes covered (Underlined)
*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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