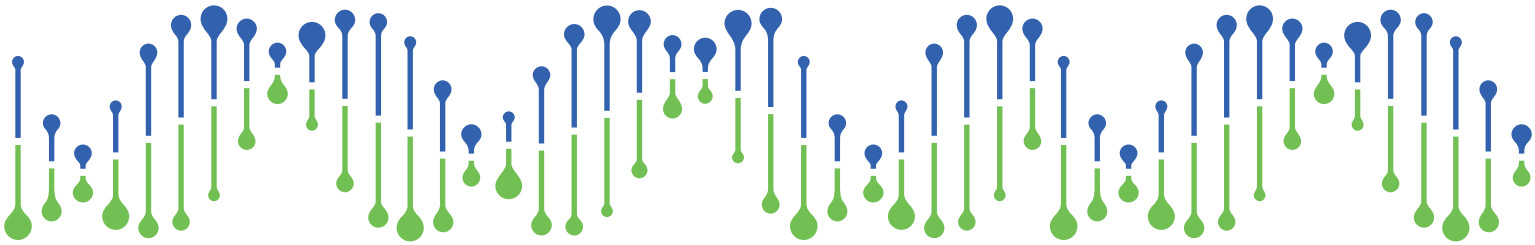

Cell3™ Target: Pan-Cancer (524), TMB, MSI panel

An NGS panel of 524 oncogenes that allows you to profile and stratify all common cancers and predict response to immunotherapy.

Highlights

Comprehensive 524 gene Pan-Cancer panel

Pan-Cancer comprehensive design allows for a streamlined laboratory workflow, allowing processing of all oncology samples through a single, simple workflow.

Predict positive response to immunotherapy treatment through a combined tumor genomic instability measurement: Tumor Mutational Burden (TMB) and MicroSatellite Instability (MSI) analysis within a single Pan-Cancer panel

Using a 1.58 Mb exon focused design, this Pan-Cancer panel has been designed with analysis of both TMB and MSI in mind and our Cell3 Target library prep makes this panel ideal for measuring TMB in either FFPE or ctDNA.

Cell-Free DNA (ctDNA) and FFPE optimized target enrichment system

Developed for, and validated on, ctDNA to enable genomic analysis of liquid biopsy using a comprehensive Pan-Cancer panel, also validated on FFPE to allow genomic analysis and combined TMB / MSI profiling in either the primary or metastatic biopsies.

We have it covered, exon focused design also covers key intronic and promoter regions

The Pan-Cancer panel was carefully selected to cover all relevant genes and regions from >500 oncogenes and allows for confident calling of targeted SNV, Indels, fusions, translocations and copy number variation.

Introduction

Immunotherapy treatment, such as checkpoint inhibitors, show great potential across a number of cancers including melanoma, non-small cell lung cancer (NSCLC), bladder cancer and kidney cancer among others. However only a subset of patients will benefit and so the need for positive biomarkers for response to immunotherapy are needed.

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Tumor genomic instability has been shown to correlate positively with immunotherapy response and two genomic biomarkers of tumor genomic instability are known: Micro Satellite Instability (MSI) and Tumor Mutational Burden (TMB). Recently the FDA has approved MSI-H (high MSI) as an approved biomarker of likely response to immunotherapy.

The overall load of somatic mutations in the tumor, or tumor mutational burden (TMB), has become increasingly utilized as a biomarker for response prediction. Numerous clinical studies have demonstrated that higher mutational burden correlates to improved survival benefits in patients receiving checkpoint inhibitor therapies for cancers such as melanoma, colon, and NSCLC. Recent data from clinical trials such as CheckMate 227 have demonstrated that in NSCLC, higher TMB is associated with improved clinical outcomes, and there are additional trials currently underway using TMB as a biomarker.

Initial studies used whole exome sequencing (WES) as the gold standard for measuring TMB; however, cost, computational complexity, and time for WES make targeted panel sequencing more attractive for routine use at present when considering the use of TMB for predicting response to immunotherapy.

Dr. Albrecht Stenzinger, a pathologist at University Hospital in Heidelberg, Germany, and his colleagues, recently performed in-silico analysis (using combinatorial calculations and extensive simulations) of TCGA data of 8371 tumors, across 25 different cancer types, including lung, melanoma, pancreatic, breast, head, and neck among others.[1]

The authors specifically investigated the influence of gene panel size on the precision of TMB measurement by considering certain core parameters, including the confidence intervals of TMB reporting, use of all mutations versus only missense mutations, and sensitivity and specificity for detection of hypermutated tumors. Their findings were recently published in the International Journal of Cancer and their research highlights the following:

- Smaller panels result in imprecise measurement of TMB, especially for tumors with low TMB values: "The data suggests that TMB estimation usin small gene panels can be highly imprecise and thus clinically suboptimal for patient stratification and response prediction."
- TMB cut-off to identify hypermutated tumors is dependent on panel size, as well as on specific histology: "Larger gene panels are associated with reasonable cutoff values that help identify true signals from background noise in routine diagnostics."

They recommend that a panel be between 1.5 Mb to 3 Mb to balance benefits with cost, whilst also recommending using both missense and nonsense mutations to calculate TMB.

For the Nonacus Pan-Cancer panel we carefully selected 524 genes with most clinical relevance and composed of 63 genes from NCCN/FDA cancer treatment guidelines, 116 cancer driver genes and 345 genes in vital cancer signaling pathways. It is a comprehensive panel that allows the combination of genetic mutation testing and treatment recommendation.

In addition, the design while exon focused covers key intronic and promoter regions and contains a selection of genome-wide CNV probes to assist with copy number calling across the genome.

Table 1. Nonacus Pan-Cancer, (524) TMB/MSI Panel gene content, panel also includes relevant promoter regions, copy number calling probes and intronic regions for key translocations.

Comprehensive cancer panel										
ABCB1	BRD4	CRKL	ERCC3	FUBP1	INPP5D	MED13	PBRM1	RAC1	SMAD2	TNFRSF14
ABCC2	BRIP1	CRLF2	ERCC4	GABRA6	IRAK4	MEF2B	PC	RAD21	SMAD3	TNFRSF17
ABL1	BTG1	CSF1R	ERCC5	GADD45B	IRF1	MEN1	PCGF2	RAD50	SMAD4	TNFRSF19
ABL2	BTG2	CSF3R	ERG	GATA1	IRF2	MET	PDCD1	RAD51	SMAD7	TOP1
ACTB	BTK	CTCF	ERRFI1	GATA2	IRF4	MGMT	PDCD1LG2	RAF1	SMARC4	TOP2A
ACVR1B	BTLA	CTLA4	ESR1	GATA3	IRF8	MITF	PDGFB	RANBP2	SMARCB1	TP53
ADGRA2	BUB1B	CTNNA1	ESR2	GATA4	IRS2	MLH1	PDGFRA	RARA	SMC1A	TP63
ADH1B	CALR	CTNNB1	ETV1	GATA6	ITCH	MLLT10	PDGFRB	RARB	SMC3	TPMT
AIP	CARD11	CUL3	ETV4	GLI1	JAK1	MPL	PDK1	RARG	SMO	TRAF2
AKT1	CBFB	CUX1	ETV5	GNA11	JAK2	MRE11	PDKF6	RASGEF1A	SNCAIP	TRAF3
AKT2	CBL	CXCR4	EWSR1	GNA13	JAK3	MSH2	PHOX2B	RB1	SOCS1	TRAF5
AKT3	CCN6	CYLD	EXOC2	GNAQ	JARID2	MSH3	PIK3C2B	RBM10	SOS1	TRRAP
ALDH2	CCND1	CYP19A1	EXT2	GNAS	JUN	MSH6	PIK3C3	RECQL4	SOX10	TSC1
ALK	CCND2	CYP2A6	EZH2	GRIN2A	KAT6A	MST1R	PIK3CA	RELN	SOX2	TSC2
AMER1	CCND3	CYP2B6	FANCA	GRM3	KDM2B	MTHFR	PIK3CB	RET	SOX9	TSHR
AP3B1	CCNE1	CYP2C19	FANCB	GSK3B	KDM5A	MTOR	PIK3CD	RHOA	SPEN	TTF1
APC	CCT6B	CYP2C9	FANCC	GSTM1	KDM5C	MUC16	PIK3CG	RICTOR	SPOP	TUBB3
AR	CD22	CYP2D6	FANCD2	GSTP1	KDM6A	MUTYH	PIK3R1	RNF43	SPRED1	TYK2
ARAF	CD274	CYP3A4	FANCE	GSTT1	KDR	MYC	PIK3R2	ROS1	SPTA1	TYMS
ARFRP1	CD58	CYP3A5	FANCF	H3-3A	KEAP1	MYCL	PLCG2	RPS6KB1	SRC	U2AF1
ARID1A	CD70	DAXX	FANCG	HBA1	KEL	MYCN	PLK1	RPTOR	SRSF2	UGT1A1
ARID2	CD79A	DDR1	FANCL	HBA2	KIT	MYD88	PMS1	RRM1	STAG2	UNC13D
ARID5B	CD79B	DDR2	FAS	HBB	KLHL6	NBN	PMS2	RUNX1	STAT3	VEGFA
ASXL1	CDA	DDX3X	FAT1	HDAC1	KMT2A	NCOR1	POLD1	RUNX1T1	STAT4	VHL
ATM	CDC73	DHFR	FBXO11	HDAC2	KMT2B	NCSTN	POLE	RXRA	STAT5A	WEE1
ATR	CDH1	DICER1	FBXO32	HDAC4	KMT2C	NEK2	POT1	RXRB	STAT5B	WRN
ATRX	CDK10	DLG2	FBXW7	HDAC7	KMT2D	NELL2	PPM1L	RXRG	STIL	WT1
AURKA	CDK12	DNM2	FCGR2B	HGF	KRAS	NF1	PP2R1A	SBDS	STK11	XIAP
AURKB	CDK4	DNMT3A	FGF10	HNF1A	LAMA2	NF2	PRDM1	SDHA	STMN1	XPC
AXIN1	CDK6	DOT1L	FGF14	HNF1B	LCK	NFE2L2	PREX2	SDHB	STX11	XPO1
AXL	CDK8	DPYD	FGF19	HRAS	LEF1	NFKBIA	PRF1	SDHC	STXBP2	XRCC1
B2M	CDKN1A	DUSP2	FGF23	HSD3B1	LMO1	NKX2-1	PRKAR1A	SDHD	SUFU	YAP1
BAP1	CDKN1B	EBF1	FGF3	HSP90AA1	LRP1B	NOTCH1	PRKCI	SEPTIN9	SUZ12	YES1
BARD1	CDKN1C	ECT2L	FGF6	ID3	LTK	NOTCH2	PRKDC	SERP2	SYK	ZAP70
BCL2	CDKN2A	EED	FGFR1	IDH1	LYN	NPM1	PRKN	SETBP1	TAF1	ZBED4
BCL2L1	CDKN2B	EGFR	FGFR2	IDH2	LYST	NQO1	PSMB1	SETD2	TANK	ZBTB2
BCL2L11	CDKN2C	EGR1	FGFR3	IGF1R	LZTR1	NRAS	PSMB2	SF3B1	TAS2R38	ZMYM3
BCL2L2	CEBPA	EP300	FGFR4	IGF2	MAGI2	NRG1	PSMB5	SGK1	TEK	ZNF217
BCL6	CEP57	EPCAM	FH	IKBKE	MAP2K1	NSD1	PSMD1	SH2D1A	TEKT4	ZNF703
BCOR	CHD2	EPHA3	FIP1L1	IKZF1	MAP2K2	NT5C2	PSMD2	SHH	TENT5C	ZRSR2
BCORL1	CHD4	EPHA5	FLCN	IKZF2	MAP2K4	NTRK1	PTCH1	SHOC2	TERC	
BCR	CHD7	EPHA7	FLT1	IKZF3	MAP3K1	NTRK2	PTEN	SLC22A1	TERT	
BIRC3	CHEK1	EPHB1	FLT3	IL2RA	MAPK1	NTRK3	PTGFR	SLC22A2	TET2	
BLM	CHEK2	ERBB2	FLT4	IL2RB	MCL1	NUP93	PTPN11	SLC31A1	TGFBR2	
BMPR1A	CHIC2	ERBB3	FOXL2	IL2RG	MDM2	PAG1	PTPN2	SLC34A2	TLE1	
BRAF	CIC	ERBB4	FOXP1	IL7R	MDM4	PAK3	PTPN6	SLC45A3	TLE4	
BRCA1	CKS1B	ERCC1	FRS2	INHBA	MECOM	PALB2	PTPRO	SLCO1B1	TMPRSS2	
BRCA2	CREBBP	ERCC2	FSTL5	INPP4B	MED12	PAX5	QKI	SLIT2	TNFAIP3	

Datasheet

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Summary

- Cell3™ Target offers a quick and flexible protocol for targeted enrichment of selected regions ahead of Illumina Next Generation Sequencing
- Validated for cell-free DNA (ctDNA) as well as FFPE / FF tissue and genomic DNA
- Use of unique molecular identifiers and unique dual indexes up to (upto 384 indexes) allows highly sensitive variant calling by removing PCR / sequencing errors and allowing removal of index hopping, while catering for even the highest throughput laboratories

Learn more

To learn more about Cell3™ Target and to download the protocols, application notes, and white papers please visit: www.nonacus.com

References

1. https://doi.org/10.1002/ijc.32002 Endris V, Buchhalter I, Allgäuer M et al. Measurement of tumor mutational burden (TMB) in routine molecular diagnostics: In-silico and real-life analysis of three larger gene panels. Int J Cancer 2019; **144**: 2303– 2312.

Ordering information

All Cell3™ Target panels are available with three fragmentation options:

A = Non-fragmentation eg (cffDNA/ctDNA),

B = Fragmentation eg gDNA or FFPE,

C = Both Fragmentation and Non-Fragmentation (half of each)

Product	Catalogue No.	
Cell3™ Target Pan-Cancer (524), Tumor Mutational Burden/MSI Panel, (16 samples)	C3299TM	(options A/B/C)
Cell3™ Target Pan-Cancer (524), Tumor Mutational Burden/MSI Panel, (96 samples)	C3300TM	(options A/B/C)

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