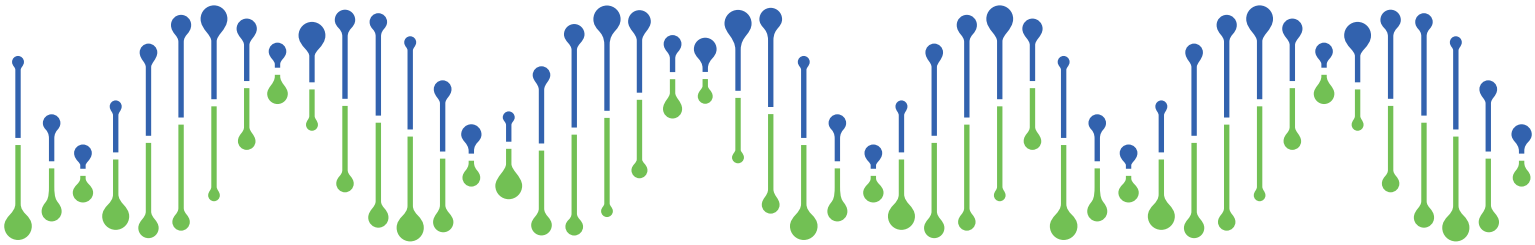

Cell3™ Target: Pan-Cancer (524), TMB, MSI panel

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	BRIP1	CRLF2	ERCC3	FRS2	IL7R	MED12	PAG1	PTPN11	SLC31A1	TLE4
ABCC2	BTG1	CSF1R	ERCC4	FSTL5	INHBA	MED13	PAK3	PTPN2	SLC34A2	TMPRSS2
ABL1	BTG2	CSF3R	ERCC5	FUBP1	INPP4B	MEF2B	PALB2	PTPN6	SLC45A3	TNFAIP3
ABL2	BTK	CTCF	ERG	GABRA6	INPP5D	MEN1	PARK2	PTPRO	SLCO1B1	TNFRSF14
ACTB	BTLA	CTLA4	ERRFI1	GADD45B	IRAK4	MET	PAX5	QKI	SLIT2	TNFRSF17
ACVR1B	BUB1B	CTNNA1	ESR1	GATA1	IRF1	MGMT	PBRM1	RAC1	SMAD2	TNFRSF19
ADH1B	C11orf30	CTNNB1	ESR2	GATA2	IRF2	MITF	PC	RAD21	SMAD3	TOP1
AIP	CALR	CUL3	ETV1	GATA3	IRF4	MLH1	PCGF2	RAD50	SMAD4	TOP2A
AKT1	CARD11	CUX1	ETV4	GATA4	IRF8	MLL	PDCD1	RAD51	SMAD7	TP53
AKT2	CBFB	CXCR4	ETV5	GATA6	IRS2	MLL2	PDCD1LG2	RAF1	SMARCA4	TP63
AKT3	CBL	CYLD	EWSR1	GU1	ITCH	MLLT10	PDGFB	RANBP2	SMARCB1	TPMT
ALDH2	CCND1	CYP19A1	EXOC2	GNA11	JAK1	MPL	PDGFRA	RARA	SMC1A	TRAF2
ALK	CCND2	CYP2A6	EXT2	GNA13	JAK2	MRE11A	PDGFRB	RARB	SMC3	TRAF3
AMER1	CCND3	CYP2B6	EZH2	GNAQ	JAK3	MSH2	PDK1	RARG	SMO	TRAF5
AP3B1	CCNE1	CYP2C19	FAM123B	GNAS	JARID2	MSH3	PHF6	RASGEF1A	SNCAIP	TRRAP
APC	CCT6B	CYP2C9	FAM46C	GPR124	JUN	MSH6	PHOX2B	RB1	SOCS1	TSC1
AR	CD22	CYP2D6	FANCA	GRIN2A	KDM2B	MST1R	PICK3R1	RBM10	SOS1	TSC2
ARAF	CD274	CYP3A4	FANCB	GRM3	KDM5A	MTHFR	PIK3C2B	RECQL4	SOX10	TSHR
ARFRP1	CD58	CYP3A5	FANCC	GSK3B	KDM5C	MTOR	PIK3C3	RELN	SOX2	TTF1
ARID1A	CD70	DAXX	FANCD2	GSTM1	KDM6A	MUC16	PIK3CA	RET	SOX9	TUBB3
AR1D2	CD79A	DDR1	FANCE	GSTP1	KDR	MUTYH	PIK3CB	RHOA	SPEN	TYK2
AR1D5B	CD79B	DDR2	FANCF	GSTT1	KEAP1	MYC	PIK3CD	RICTOR	SPOP	TYMS
ASXL1	CDA	DDX3X	FANCG	H3F3A	KEL	MYCL1	PIK3CG	RNF43	SPRED1	U2AF1
ATM	CDC73	DHFR	FANCL	HBA1	LIT	MYCN	PIK3R1	ROS1	SPTA1	UGT1A1
ATR	CDH1	DICER1	FAS	HBA2	KLHL6	MYD88	PIK3R2	RPS6KB1	SRC	UNC13D
ATRX	CDK10	DLG2	FAT1	HBB	KMT2A	MYST3	PLCG2	RPTOR	SRSF2	VEGFA
AURKA	CDK12	DMNT3A	FBXO11	HDAC1	KMT2B	NBN	PLK1	RRM1	STAG2	VHL
AURKB	CDK4	DNM2	FBXO32	HDAC2	KMT2C	NCOR1	PMS1	RUNX1	STAT3	WEE1
AXIN1	CDK6	DNMT3A	FBXW7	HDAC4	KRAS	NCSTN	PMS2	RUNX1T1	STAT4	WISP3
AXL	CDK8	DOT1L	FCGR2B	HDAC7	LAMA2	NEK2	POLD1	RXRA	STAT5A	WRN
B2M	CDKN1A	DPYD	FGF10	HGF	LCK	NELL2	POLE	RXRB	STAT5B	WT1
BAP1	CDKN1B	DUSP2	FGF14	HNF1A	LEF1	NF1	POT1	RXRG	STIL	XIAP
BARD1	CDKN1C	EBF1	FGF19	HNF1B	LMO1	NF2	PPM1L	SBDS	STK11	XPC
BCL2	CDKN2A	ECT2L	FGF23	HRAS	LRP1B	NFE2L2	PPP2R1A	SDHA	STMN1	XPO1
BCL2L1	CDKN2B	EED	FGF3	HSD3B1	LTK	NFKBIA	PRDM1	SDHB	STX11	XRCC1
BCL2L11	CDKN2C	EGFR	FGF6	HSP90AA1	LYN	NKX2-1	PREX2	SDHC	STXBP2	YAP1
BCL2L2	CEBPA	EGR1	FGFR1	ID3	LYST	NOTCH1	PRF1	SDHD	SUFU	YES1
BCL6	CEP57	EP300	FGFR2	IDH1	LZTR1	NOTCH2	PRKAR1A	SEPT.9	SUZ12	ZAP70
BCOR	CHD2	EPCAM	FGFR3	IDH2	MAGI2	NPM1	PRKCI	SERP2	SYK	ZBED4
BCORL1	CHD4	EPHA3	FGFR4	IGF1R	MAP2K1	NQO1	PRKDC	SETBP1	TAF1	ZBTB2
BCR	CHD7	EPHA5	FH	IGF2	MAP2K2	NRAS	PSMB1	SETD2	TAS2R38	ZMYM3
BIRC3	CHEK1	EPHA7	FIP1L1	IKBKE	MAP2K4	NRG1	PSMB2	SF3B1	TEK	ZNF217
BLM	CHEK2	EPHB1	FLCM	IKZF1	MAP3K1	NSD1	PSMB5	SGK1	TEKT4	ZNF703
BMPR1A	CHIC2	ERBB2	FLT1	IKZF2	MAPK1	NT5C2	PSMD1	SH2D1A	TERC	ZRSR2
BRAF	CIC	ERBB3	FLT3	IKZF3	MCL1	NTRK1	PSMD2	SHH	TERT	
BRCA1	CKS1B	ERBB4	FLT4	IL2RA	MDM2	NTRK2	PTCH1	SHOC2	TET2	
BRCA2	CREBBP	ERCC1	FOXL2	IL2RB	MDM4	NTRK3	PTEN	SLC22A1	TGFBR2	
BRD4	CRKL	ERCC2	FOXP1	IL2RG	MECOM	NUP93	PTGFR	SLC22A2	TLE1	

Datasheet

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

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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