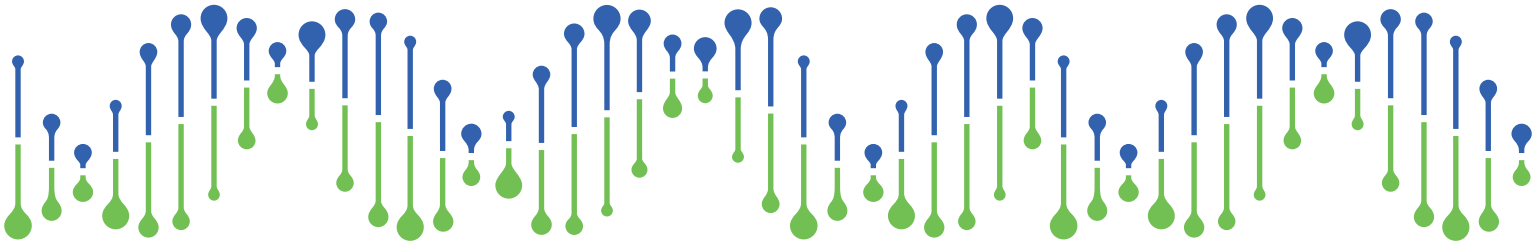
Datasheet
Hereditary Cancer Panel



Cell3™ Target: Hereditary Cancer Panel

A comprehensive NGS sequencing panel for analysing germline mutations associated with hereditary cancers

Highlights

Comprehensive content for assessing germine mutations

Target 129 genes associated with a predisposition for hereditary cancer including breast, ovarian, uterine, prostate and gastrointestinal cancers as well as rarer hereditary cancers and paediatric cancers like phaeochromocytoma and Wilms tumor.

Streamlined workflow

Validate and run one workflow for all hereditary cancers regardless of cancer type and sample input amount or type.

Robust calling of all variants

Confidently call all variants including SNVs, Indels and CNVs with high recall and precision.

Lower sequencing costs

Generate more sequence per sample with high on-target rates, superior uniformity of coverage and low levels of duplication.

Introduction

Hereditary cancers account for around 5-10%[1] of all cancers and include cancers of the breast, ovary, uterus, prostate, and gastrointestinal system, which includes the stomach, colon, rectum, small bowel, and pancreas.

Genetic testing to identify an inherited variant associated with cancer can provide a cancer risk assessment for an individual and guide the implementation of additional screening and surveillance if necessary. This in turn may result in an early diagnosis and help guide treatment.

As well as helping improve outcomes for patients diagnosed with hereditary cancer, testing for inherited variants associated with cancer may also help guide additional screening and early diagnosis of at risk relatives.

By using a multi-cancer panel to screen for germline mutations, researchers can profile known genetic associations for hereditary cancer regardless of cancer type. This maximises diagnostic yield for individuals with a personal or family history of mixed cancers affecting multiple organ systems or those with an unknown family history.

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Cell3™ Target Hereditary Cancer Panel

The Cell3™ Target Hereditary Cancer Panel is a targeted enrichment panel for NGS sequencing. The panel has been designed to target germline mutations in 129 genes associated with an increased risk of developing hereditary cancer. These genes have been selected to cover not only the common hereditary cancers listed above but also some of the rarer hereditary cancers like Phaeochromocytoma and paediatric cancers like Wilms tumor.

Table 1: Hereditary cancer panel gene content (see appendix)

ACD	EGFR	HOXB13	POLE	SUFU
ACVRL1	ENG	HRAS	POLH	TERC
AIP	EPCAM	KCNJ5	POT1	TERF2IP
ALK	ERCC1	KIF1B	PRF1	TERT
APC	ERCC2	KIT	PRKAR1A	TMEM127
ATM	ERCC3	MAX	PTCH1	TP53
AXIN2	ERCC4	MC1R	PTEN	TRIM28
BAP1	ERCC5	MEN1	RAD50	TSC1
BARD1	EXO1	MET	RAD51	TSC2
BLM	EXT1	MITF	RAD51B	VHL
BMPR1A	EXT2	MLH1	RAD51C	WRN
BRCA1	EZH2	MRE11	RAD51D	WT1
BRCA2	FANCA	MSDH2	RB1	XPA
BRIP1	FANCB	MSH3	RECQL4	XPC
BUB1B	FANCC	MSH6	RET	
CDC73	FACD2	MUTYH	RHBDF2	
CDH1	FANCE	NBN	RUNX1	
CDK4	FANCF	NF1	SBDS	
CDKN1B	FANCG	NF2	SDHA	
CDKN1C	FANCI	NSD1	SDHAF2	
CDKN2A	FANCM	NTHL1	SDHB	
CEBPA	FH	PLB2	SDHC	
CHEK2	FLCN	PALLD	SDHD	
CTR9	GALNT12	PDGFRA	SLX4	
CYLD	GATA2	PHOX2B	SMARCA4	
DDB2	GPC3	PMS1	SMARCB1	
DICER1	GREM1	PMS2	SMARCE1	
DIS3L2	HNF1A	POLD1	STK11	

Superior precision and recall ensure confident calling of SNV, CNV and indel variants

To demonstrate variant calling performance of the Cell3™ Target Hereditary Cancer panel, the precision and recall for single nucleotide variants (SNVs) and insertion-deletion mutations (indels) were tested alongside two competitor panels on commercially available reference standards containing multiple variants. The Nonacus panel showed excellent recall for SNVs (Figure 1), and indels (Figure 2), with both higher than either of the competitors' products.

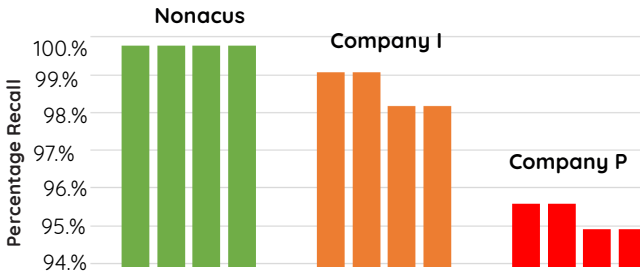

Figure 1: Nonacus Hereditary cancer panel delivers a mean SNV recall of 99.78% across four replicates outperforming Company I and Company P.

[Cell line control sample NA24385 (GIAB) was sequenced using each panel. Comparable data was generated by randomly down sampling the available sequencing reads for all samples to 100x mean coverage depth and analysing through the Nonacus analysis pipeline].

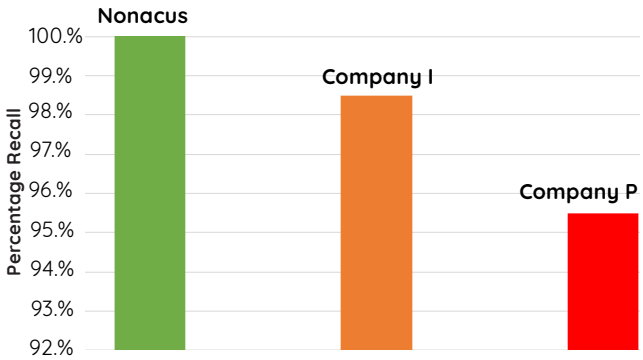

Figure 2: The Nonacus Hereditary Cancer Panel delivers the highest average indel recall outperforming Company I and Company P.

[Cell line Seraseq® Inherited Cancer DNA Mix v1 was used to compare the indel calling between three products. Samples were run in replicate (n=4) and comparable data was generated by randomly down sampling all samples to 100x mean depth and analysing through Nonacus analysis pipeline].

To evaluate the sensitivity of CNV genotyping with the Cell3™ Target Hereditary Cancer Panel, the panel was run using NIBSC Lynch Syndrome MLPA cell lines. All CNVs were detected with 100% recall and precision when using sex matched control pools (Table 2).

Table 2: The Nonacus Cell3™ Target Hereditary Cancer panel confidently calls CNVs with 100% precision and 100% recall.

CNV	Genotypic sex	CNV type	Detected	Recall	Precision
Copy Normal	male	copy neutral	YES	100%	100%
MSH2 deletion exons 1-6, heterozygous	male	multi-exon deletion	YES	100%	100%
MSH2 deletion exon 7, heterozygous	male	single exon deletion	YES	100%	100%
MSH2 deletion exons 1-2, heterozygous	female	multi-exon deletion	YES	100%	100%
MSH2 deletion, exon 1, heterozygous	male	single exon deletion	YES	100%	100%
MLH1 exon 13 amplification (3 or more copies)	female	multi-exon amplification	YES	100%	100%

High on-target rates and uniform coverage deliver more efficient sequencing

The Cell3™ Target Hereditary Cancer panel design delivers a higher percentage of on-target reads (with padding at 150 bp) when compared with a leading competitor's panel (Figure 3).

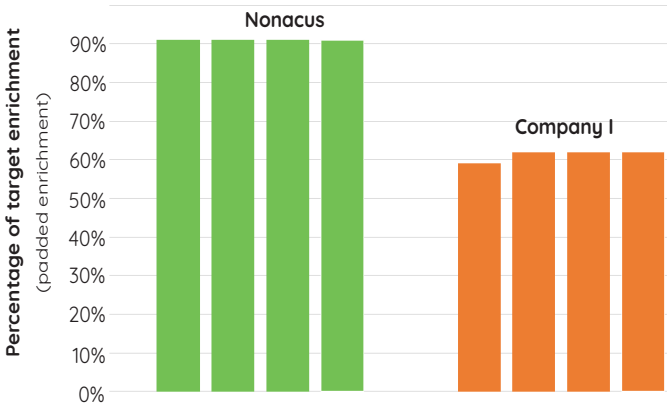

Figure 3: Percentage of on or near target reads (padding of 150bp) for Cell3™ Target Hereditary Cancer Panel and Company I.

[Samples were run in replicate (n=4) across NA24385 (GIAB) and SeraSeq cell line control samples. Percent on or near bait value was calculated using Sentieon HSMetrics].

The panel also resulted in lower duplication rates and more consistent vertical coverage with 98% of targets covered at 30x or more (Table 3). This uniformity of coverage combined with a low duplication rate and high percentage of on target reads delivers exceptional performance resulting in less wasted sequencing.

Table 3: Performance data for the Nonacus Cell3™ Target Hereditary Cancer Panel compared with a leading competitor panel.

[Samples were run in replicate (n=4) across NA24385(GIAB) and SeraSeq cell line control samples. BAM files were down sampled to 100X mean coverage for comparison. Data was generated using the Nonacus analysis pipleine].

	Nonacus	Company I
Panel size (kb)	644	403
MB required for mean 100x coverage	78.1 MB	116.6 MB
Percentage coverage >30x	98%	96%
Percent padded read enrichment	90.99%	61.51%
Percent duplication	3.00%	8.99%

The impact of this on sequencing efficiency can be seen in Table 4. Using this panel, researchers can generate more sequencing data per sample or run up to 50% more samples, with the same sequencing flow cell, than the leading competitor's product.

Table 4: Estimated maximum number of samples per flow cell to achieve 100x mean depth of coverage based on 2 x 150bp PE sequencing calculated based on data obtained in Table 3.

Sequencer	Flow Cell	Hereditary Cancer Panel	Samples/ Flow cell
MiSeq	v3.0	Nonacus	96
		Company I	64
	v2.0	Nonacus	58
		Company I	39
	v2 Nano	Nonacus	4
		Company I	3
	v2 Micro	Nonacus	15
		Company I	10

Cell3 Target products are compatible with all current Illumina Sequencers, please contact us for sample quantity on NextSeq or NovaSeq.

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Streamlined workflow

Rather than running multiple panels to cover different cancer syndromes, the Cell3™ Target Hereditary Cancer panel enables laboratories to validate and run just one workflow for profiling all hereditary cancer types. In addition to maximising diagnostic yield, the Cell3™ Target Hereditary Cancer panel simplifies laboratory workflows reducing laboratory validation and operating costs.

Multi-cancer panels also enable the creation of virtual sub panels for analysis of specific cancers if comprehensive analysis is not appropriate.

Quick and easy protocols

The Cell3™ Target workflow is simple and easy. Taking less than 10 hours, with less than 2 hours hands-on time, it is designed with multiple stop points to provide flexibility within laboratory processing. Library preparation can be run manually or automated up to 96 samples in a single run.

Indexes are available for up to 384 samples to allow for flexible batch sizes and scalability across all Illumina benchtop sequencers

Summary

The Cell3™ Target Hereditary Cancer Panel is a hybrid-capture panel designed to target germline mutations in 129 genes associated with an increased risk of developing hereditary cancer. Its robust performance enables laboratories to confidently call variants including SNVs, Indels and CNVs with high recall and precision. The multi-cancer format increases diagnostic yield and simplifies laboratory workflows. The high on-target rate, low level of duplication and superior uniformity of coverage improve the efficiency of sequencing and reduce sequencing cost per sample whilst enabling more samples per flow cell.

Parameter	Specification
Enrichment method	Hybrid capture
Number of genes	129 (all exons)
Capture Panel size	644 kb
Sequencing platform	Illumina
Targets	Genes associated with hereditary cancer
Variant types	SNVs, CNVs and Indels
Input DNA requirements	10ng-200ng
Sample type	gDNA from blood, saliva, tissue or FFPE
Percent duplication	3%
Coverage uniformity (percentage of targets covered <30x)	98%
Padded read enrichment (on-target)	91%
Multiplex capability	384

Learn more

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

References

1. Ngeow, J., Eng, C. Precision medicine inheritable cancer: when somatic tumour testing and germline mutations meet. npj Genomic Med 1, 15006 (2016). https://doi.org/10.1038/npjgenmed.2015.6

Ordering information

Product	Catalogue No.
Cell3™ Target Hereditary Cancer Panel, 16 samples (Frag or Non Frag)	NGS_C3T_HCP_FR_16/ NGS_C3T_HCP_NF_16
Cell3™ Target Hereditary Cancer Panel, 96 samples (Frag or Non Frag)	NGS_C3T_HCP_FR_96/ NGS_C3T_HCP_NF_96

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Appendix: Gene list for Hereditary Cancer Panel

ACD	FANCD2	PRF1
ACVRL1	FANCE	PRKAR1A
AIP	FANCF	PTCH1
ALK	FANCG	PTEN
APC	FANCI	RAD50
ATM	FANCM	RAD51
AXIN2	FH	RAD51B
BAP1	FLCN	RAD51C
BARD1	GALNT12	RAD51D
BLM	GATA2	RB1
BMPR1A	GPC3	RECQL4
BRCA1	GREM1	RET
BRCA2	HNF1A	RHBDF2
BRIP1	HOXB13	RUNX1
BUB1B	HRAS	SBDS
CDC73	KCNJ5	SDHA
CDH1	KIF1B	SDHAF2
CDK4	KIT	SDHB
CDKN1B	MAX	SDHC
CDKN1C	MC1R	SDHD
CDKN2A	MEN1	SLX4
CEBPA	MET	SMAD4
CEP57	MITF	SMARCA4
CHEK2	MLH1	SMARCB1
CTR9	MRE11	SMARCE1
CYLD	MSDH2	STK11
DDB2	MSH3	SUFU
DICER1	MSH6	TERC
DIS3L2	MUTYH	TERF2IP
EGFR	NBN	TERT
ENG	NF1	TMEM127
EPCAM	NF2	TP53
ERCC1	NSD1	TRIM28
ERCC2	NTHL1	TSC1
ERCC3	PALB2	TSC2
ERCC4	PALLD	VHL
ERCC5	PDGFRA	WRN
EXO1	PHOX2B	WT1
EXT1	PMS1	XPA
EXT2	PMS2	XPC