

Agilent SureSelect Cancer Custom Panels

Tumor genomic profiling with customized insights

Key advantages

- Leverage globally curated cancer gene lists for custom panel design
- Guided, easy-to-use panel design software powered by machine learning
- Scalable custom cancer panels from 1 kb to 24 Mb target size
- Seamless inclusion of TMB and MSI assessment in custom cancer panel design
- Flexible data analysis options

Introduction

Agilent SureSelect Cancer Custom panels enable tumor genomic profiling with next-generation sequencing (NGS) panels customized to fit specific laboratory requirements, including the incorporation of new and emerging biomarkers. These custom panels are designed with Agilent SureDesign, a user-friendly software that offers easy access to predefined, globally curated gene lists sourced from cancer databases and leading clinical cancer researchers. The available gene lists are based on catalog DNA panels: Agilent SureSelect Cancer CGP DNA panel and tumor-specific panels (lung, colon, breast, prostate, gastric, pancreas, melanoma, kidney, and bladder).

SureSelect Cancer Custom panels are combined with library preparation and target enrichment reagents to enable detection of all key classes of somatic changes, including single nucleotide variants (SNVs), copy number variants (CNVs), insertions/deletions (indels), and translocations (TLs). Moreover, the design of these custom DNA panels supports options to include the assessment of the immuno-oncology biomarkers, tumor mutational burden (TMB) and microsatellite instability (MSI); as well as homologous recombination deficiency (HRD) assessment. For gene fusion detection, these custom panels can also be paired with the SureSelect Cancer CGP RNA assay (80 genes) and multiplexed in the same sequencing run. The SureSelect Cancer Custom panels are compatible with sequencing instruments from different vendors (Illumina, Element Biosciences, Pacific Biosciences, and MGI).

The SureSelect Cancer Custom panels work with the streamlined and high-performance Agilent SureSelect XT HS2 library preparation and target enrichment chemistry. The assays feature a fast, 90-minute hybridization step, compatibility with input as low as 10 ng, and a single-day workflow to generate sequencing-ready libraries. For optimal convenience, the assays also include enzymatic fragmentation, eliminating the need for physical shearing equipment. Maximize workflow efficiency and minimize time at the bench using the Agilent Magnis NGS Prep system, a fully automated, walkaway platform that only requires 15 minutes of hands-on time for generating sequencing-ready libraries.

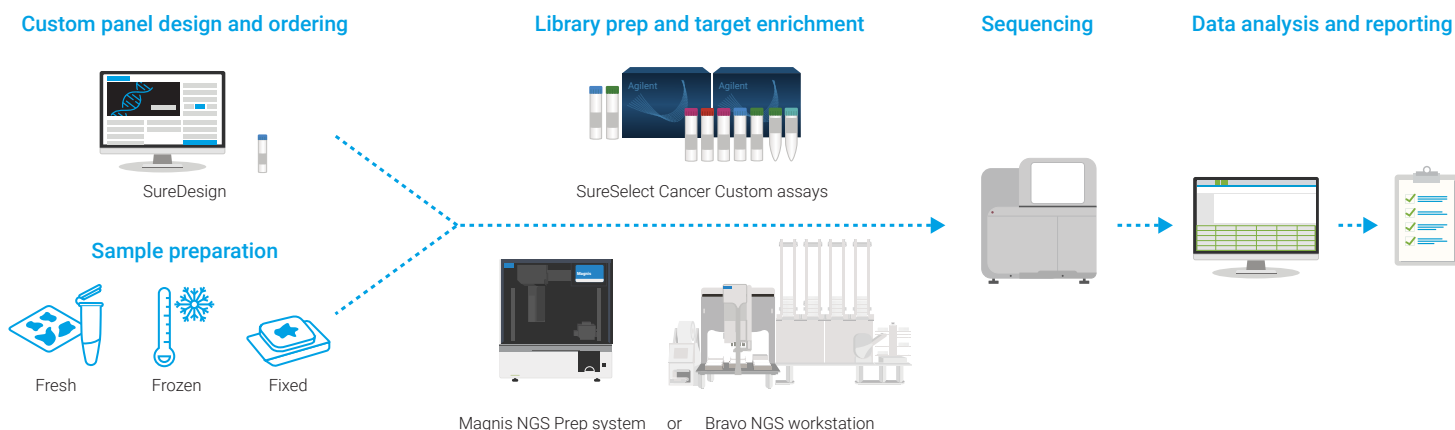


Figure 1. The NGS workflow starts with the design of a SureSelect Cancer Custom panel using SureDesign software, a web portal for probe design powered by machine learning. The workflow incorporates sample and NGS library QC using the Agilent TapeStation systems. Library preparation and target enrichment can be performed manually or automated using either the benchtop Agilent Magnis NGS Prep system, requiring only 15 minutes hands-on time, or the high-throughput Agilent Bravo NGS Workstation to generate sequencing-ready libraries. Sequencing is performed on a compatible sequencing system. Data analysis options enable flexibility to choose from Agilent Alissa Reporter, customer in-house and third-party software, such as SOPHiA GENETICS.

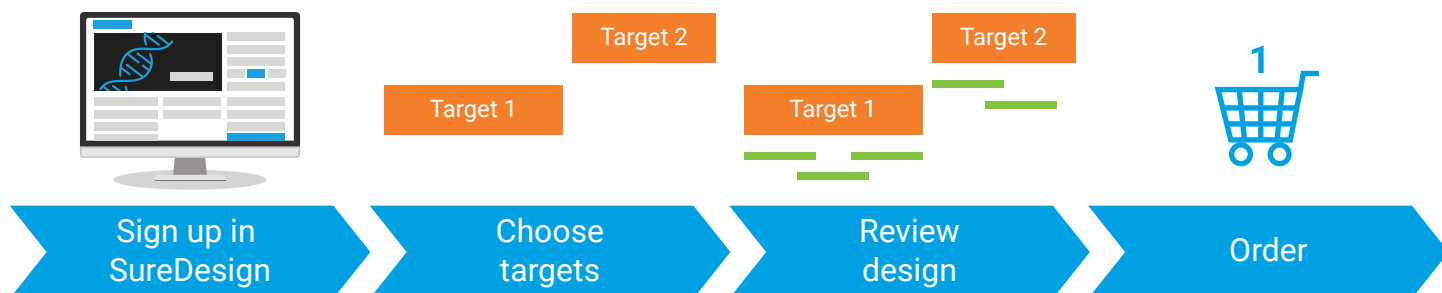


Figure 2. Design of a SureSelect Cancer Custom panel is fast and simple. Registration enables instant access to the SureDesign software. The guided design process in SureDesign offers target selection based on predefined, globally curated cancer gene lists, with the option to add your own set of genes. After design review, the software offers convenient quoting to order the newly designed SureSelect Cancer Custom panel.

A

SureDesign Help - Pre-defined Cancer Genes

SureSelect Cancer CGP Add/Review Content Pre-defined Cancer Genes

Define Design Add/Review Content Pre-defined Cancer Genes Custom Targets/Regions Select Existing Probes Finalize

* Targets: SureSelect Cancer Breast DNA Panel Search Upload Targets

ABL1	ABL2	ABR	ACVR1	ACVR1B	ACVR2A	ADGRA2	AJUBA	AKAP9	AKT1	AKT2
AKT3	ALK	ALOX12B	ALOX15B	AMER1	ANKRD11	ANKRD26	APC	APLN	AR	ARAF
ARFRP1	ARHGAP26	ARHGAP35	ARID1A	ARID1B	ARID2	ARID5B	ASXL1	ASXL2	ATM	ATR
ATRX	AURKA	AURKB	AURKC	AXIN1	AXIN2	AXL	B2M	BAP1	BARO1	BBC3
BCL10	BCL2	BCL2L1	BCL2L11	BCL2L2	BCL6	BICOR	BCORL1	BCR	BIRC2	BIRC3
BLM	BMPR1A	BRAF	BRCA1	BRCA2	BRD4	BRIP1	BTG1	BTG2	BTK	C11ORF30
CALR	CARD11	CASP8	CASR	CBFB	CBL	CBLB	CND1	CCND2	CCND3	CCNE1
CD22	CD274	CD276	CD38	CD44	CD58	CD70	CD74	CD79A	CD79B	CDK73
CDH1	CDK12	CDK2	CDK4	CDK6	CDK7	CDK8	CDKN1A	CDKN1B	CDKN1C	CDKN2A
CDKN2B	CDKN2C	CEBPA	CENPA	CFTR	CHD2	CHD4	CHD8	CHEK1	CHEK2	CIC
CIT1A	CKS1B	COL17A1	CPA1	CRBN	CREBBP	CRKL	CRLF2	CSAD	CSF1R	CSF3R
CSNK1A1	CTCF	CTLA4	CTNNA1	CTNNA1	CTRC	CUL3	CUL4A	CUL4B	CUX1	CXCR4
CYLD	CYP17A1	DAXX	DCUN1D1	DDR1	DDR2	DDX3X	DDX41	DDX5	DEFB134	DHX15
DHX9	DICER1	DIS3	DIS3L2	DLX1	DNAJB1	DNMT1	DNMT3A	DNMT3B	DOT1L	DPYD
E2F3	EED	EGFL7	EGFR	EIF1AX	EIF4A2	EIF4E	ELAC2	ELF3	EMIL4	EP300
EPCAM	EPHA2	EPHA3	EPHA5	EPHA7	EPHB1	EPHB2	EPHB4	ERBB2	ERBB3	ERBB4
ERCC1	ERCC2	ERCC3	ERCC4	ERCC5	ERG	ERF1	ESR1	ESR2	ETV1	ETV1
ETV4	ETV5	ETV6	EWSR1	EZH2	EZR	FAM175A	FAM46C	FANCA	FANCC	FANCD2

Selected Targets: 53/679

Select All Clear

Cancel Back Next

Figure 3. SureDesign 8.0 software enables the fast and easy design of SureSelect Cancer Custom panels. **A.** SureDesign guides users in designing SureSelect Cancer Custom panels with target selection from globally curated lists of genes derived from a catalog pan-cancer panel (679 genes from SureSelect Cancer CGP DNA panel), nine tumor-specific panels (~50 genes each), and user gene lists. **B.** SureDesign also features options to include the assessment of the immunology biomarkers, TMB and MSI, in the design of the SureSelect Cancer Custom panel. For TMB measurement, exonic content of at least 1 Mb is strongly recommended.¹ For MSI detection, a set of probes covering microsatellite sites will be added to the custom panel design. **C.** After the custom design is reviewed, users can obtain quotes for the SureSelect Cancer Custom panel along with the required library preparation and target enrichment kits in SureDesign.

B

SureDesign Help - Define Design

SureSelect Cancer CGP Define Design

Define Design Add/Review Content Pre-defined Cancer Genes Custom Targets/Regions Select Existing Probes Finalize

Design Name: 240308 CGP Design

* Species: H. sapiens Select

Build: UCSC hg38, GRCh38, December 2013

* Create In: Agilent Select

☒ TMB Calculation ?

☒ MSI Detection ?

Description:

Keywords:

* Design Name: 240308 CGP Design

* Species: H. sapiens Select

Build: UCSC hg38, GRCh38, December 2013

* Create In: Agilent Select

☒ TMB Calculation ?

☒ MSI Detection ?

Cancel Next

C

SureDesign Help - Order

SureSelect Cancer CGP Order

Design Name: 240222 Demonstration

Design ID: A2170241

* Quantity: 1

Automation Kit: ☒ None ☐ Bravo ☐ Magnis

Sequencing Platform: HiSeq

Reagent Kit: XT HS2, index 1-16

Sample size: 16

Beads: Purification and capture beads included in the kit

Design Part Number: 5282-0164

Kit Part Number: G9982A

Workgroup Name: Agilent Technologies

Company Name: Internal

Company Number: Internal

You are currently logged into SureDesign.

SureDesign shares a shopping cart with the Agilent Genomics website. To purchase online, you also need to be registered with that site.

To check-out, click the cart icon, and you will be transferred to the Agilent Genomics page. You must be logged in to see your discounted prices.

Request a Quote Cancel

Excellent Target Coverage for Reliable Results

Table 1. Five custom panels were designed in SureDesign 8.0 as SureSelect Cancer Custom panels. The design of the Custom CGP panel covered a large subset of genes from the catalog pan-cancer panel, SureSelect Cancer CGP DNA panel. The four smaller panels were designed based the respective tumor-specific gene lists in SureDesign. For each panel, the target sizes and approximate number of genes are shown in the table. These panels were made-to-order and used in the assays described in Figure 4 and Tables 2 and 3.

SureSelect Cancer Custom Panel	Size (Mb)	Number of genes
Custom CGP panel	1.42	~300
Custom breast panel	0.45	~50
Custom lung panel	0.53	~50
Custom gastric panel	0.36	~50
Custom bladder panel	0.33	~50

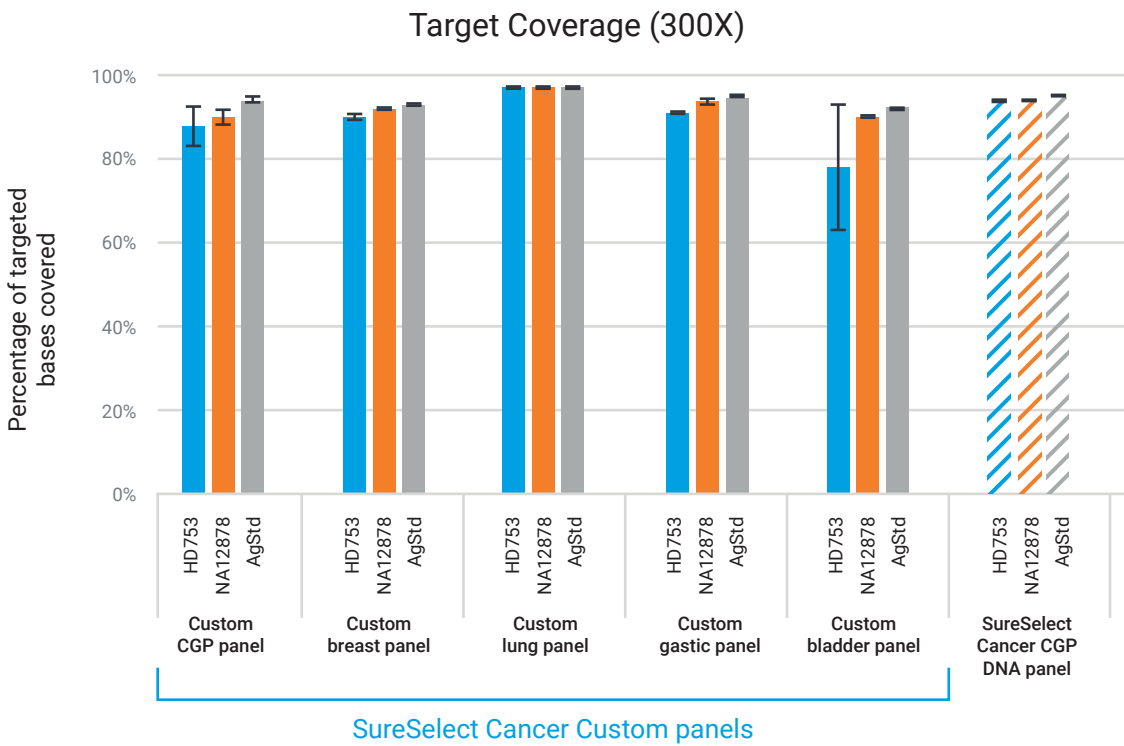


Figure 4. Excellent enrichment efficiency from the SureSelect Cancer Custom panels enables deep target coverage. The fraction of targeted bases that have greater than or equal to 300X coverage is shown for each assay using the SureSelect Cancer Custom panels; the catalog SureSelect Cancer CGP assay (p/n G9967B) was also included as a reference. The SureSelect Cancer Custom assays show high target coverage, with over 75% of the fraction of targeted bases exhibiting coverage of greater than or equal to 300X. The high coverage, which depends on the panel content and size, shows the precision and efficacy of the SureSelect Cancer Custom panels in capturing the targeted genomic regions of interest. Samples tested were reference samples from Horizon and Agilent Technologies: Horizon Discovery Structural Multiplex Reference Standard gDNA (HD753); Coriell Institute HapMap DNA NA12878; and Agilent OneSeq Reference DNA, Female (p/n 5190-8850, AgStd). Fifty nanograms of DNA from the indicated reference samples were processed using Agilent SureSelect XT HS2 library preparation reagents with enzymatic shearing, as recommended for the SureSelect Cancer assays and sequenced on the Illumina NovaSeq 6000 (2 x 150 bp reads). Data were down sampled to ~2000X sequencing coverage (2 x 150 bp reads) for analysis. Sequencing metrics were determined using the target file for each panel.

Consistent Detection of Key Somatic Variant Classes

Table 2. The SureSelect Cancer Custom panels provide reproducible detection of single nucleotide variants (SNVs), insertions (ins.), deletions (del.), and copy number variation (CNV) down to 5% variant allele frequency (VAF); the catalog SureSelect Cancer CGP DNA panel was also included as reference. Fifty nanograms of the Horizon Discovery Structural Multiplex Reference Standard gDNA (HD753) was assayed and sequenced on the Illumina NovaSeq6000 Sequencer. Data were down sampled to ~2000X sequencing coverage (2 x 150 bp reads) for analysis and analyzed for variants using an internally developed SNP caller. Measured allele frequency represents the average of the three replicate assays. All variants were detected in all three replicates. Gray boxes represent genes that are not targeted in the respective SureSelect Cancer Custom panels.

Gene	Variant	Variant Type	Expected VAF	Measured Variant Allelic Frequency (VAF)					
				SureSelect Cancer CGP Assay	SureSelect Cancer Custom Assays				
					Custom CGP Panel	Custom Breast Panel	Custom Lung Panel	Custom Gastric Panel	Custom Bladder Panel
AKT1	E17K	SNV	5.0%	5.5%	5.6%	4.7%	3.8%		5.0%
BRCA2	K1691Nfs*15	1 bp del.	5.6%	4.5%		7.5%			
BRAF	V600E	SNV	18.2%	15.8%	15.9%	16.2%	16.2%		15.0%
EGFR	G719S	SNV	5.3%	4.3%	5.2%		5.5%		
EGFR	ΔE746 - A750	9 bp ins.	5.0%	1.8%	2.1%		2.9%		
FBXW7	S668Vfs*39	1 bp del.	5.6%	4.7%	4.3%	5.6%		4.8%	
FLT3	P986Afs*27	2 bp del.	5.6%	5.0%	6.8%				
GNA11	Q209L	SNV	5.6%	5.5%	5.6%				
KRAS	G13D	SNV	5.6%	4.9%	5.8%	4.6%	5.1%	4.5%	5.0%
MET	L238Yfs*25	1 bp del.	2.5%	2.9%	2.4%	3.0%	2.9%		
PIK3CA	E545K	SNV	5.6%	4.6%	5.4%	4.0%	4.4%	5.0%	5.0%
PIK3CA	H1047R	SNV	16.7%	14.7%	14.9%	15.7%	14.3%	15.1%	15.0%
MET	Amplification	CNV	4.5 copies	5.0 copies	4.0 copies	3.7 copies	3.3 copies	3.0 copies	3.0 copies
N-MYC	Amplification	CNV	9.5 copies	9.0 copies	7.0 copies	7.3 copies	8.0 copies	8.0 copies	7.0 copies

Table 3. The SureSelect Cancer Custom panel design approach enables confident detection of the immuno-oncology biomarkers, TMB and MSI. Tumor samples with high MSI and TMB status show better response to immunotherapy. Samples were procured from commercial vendors and the reference MSI status is shown in the second column. High concordance was observed between Custom CGP panel and catalog SureSelect Cancer CGP assay: microsatellite-stable (MSS) samples (Colon_1, Bladder_1, Colon_2) showed low TMB and MSI scores, whereas MSI-high samples (Colon_3, HD753) showed high TMB and MSI scores. Score determination was performed using Agilent internal analysis software.

Sample ID	Reference MSI Status	Custom CGP Panel				SureSelect Cancer CGP Assay	
		TMB Score	TMB Status	MSI Score	MSI Status	TMB Score	MSI Score
Colon_1	MSS	5.0	Low	15	MSS	7.5	16
Bladder_1	MSS	8.0	Low	14	MSS	13.0	15
Colon_2	MSS	9.3	Low	13	MSS	8.0	14
Colon_3	MSI-H	56.3	High	61	MSI-H	54.5	64
HD753	MSI-H	210.0	High	75	MSI-H	195.0	77

Ordering Information

SureSelect Cancer Custom Panel Probes—Probes only			
Product Description	16 Rxns	96 Rxns	96 Rxns Auto*
SureSelect Cancer Custom Panel Probes, DNA, Tier 1 (up to 499 kbp or 60,500 probes)	5282-0164	5282-0165	5282-0166
SureSelect Cancer Custom Panel Probes, DNA, Tier 2 (0.5 to 2.999 Mbp or up to 121,000 probes)	5282-0167	5282-0168	5282-0169
SureSelect Cancer CGP DNA Catalog + Tier 1 Custom Panel Probes	5282-0170	5282-0171	5282-0172
SureSelect Custom Probes, Tier 3 (3.0 to 5.999 Mbp or up to 181,500 probes)	5191-6910	5191-6911	5191-6912
SureSelect Custom Probes, Tier 4 (6.0 to 11.999 Mbp or up to 242,000 probes)	5191-6915	5191-6916	5191-6917
SureSelect Custom Probes, Tier 5 (12.0 to 24 Mbp or up to 363,000 probes)	5191-6920	5191-6921	5191-6922
SureSelect Cancer Custom Assays—Kits for manual library preparation and target enrichment			
Product Description	16 Rxns	96 Rxns	96 Rxns Auto*
SureSelect XT HS2 DNA Starter Kit with Index Primer Pairs 1 to 16, 16 reactions**	G9982A		
SureSelect XT HS2 DNA Reagent Kit with AMPure® XP/Streptavidin Beads and Index Primer Pairs 1 to 96, 96 reactions		G9984A	
SureSelect Enzymatic Fragmentation Kit, 96 reactions		5191-4080	5191-6764
SureSelect Cancer Custom Assays—Complete kits for library preparation and target enrichment, including custom probes, for use with the automated Magnis NGS Prep system			
Product Description	32 Rxns Auto	96 Rxns Auto	
Magnis SureSelect Cancer XT HS2 DNA Custom Assay, Tier 1	G9777E#010	G9777F#010	
Magnis SureSelect Cancer XT HS2 DNA Custom Assay, Tier 2	G9777E#020	G9777F#020	
Magnis SureSelect Cancer XT HS2 DNA Custom Assay, Tier 3	G9777E#030	G9777F#030	
Magnis SureSelect Cancer XT HS2 DNA Custom Assay, Tier 4	G9777E#040	G9777F#040	
Magnis SureSelect Cancer XT HS2 DNA Custom Assay, Tier 5	G9777E#050	G9777F#050	
SureSelect Cancer CGP RNA Assay—Manual library preparation and target enrichment kits			
Product Description	16 Rxns	96 Rxns	
SureSelect Cancer CGP Assay RNA Kit	G9968A	G9968B	
SureSelect Enzymatic Fragmentation Kit	5191-4079	5191-4080	
SureSelect Cancer CGP RNA Assay—Automation kits for library preparation and target enrichment			
Product Description	32 Rxns Auto	96 Rxns Auto	
Magnis SureSelect Cancer CGP XT HS2 RNA Kit	G9777C	G9777D	
SureSelect Cancer CGP Assay RNA Kit, Auto		G9968C*	
SureSelect Enzymatic Fragmentation Kit, Auto		5191-6764*	

*Compatible with the automated Bravo NGS workstation and other liquid handling systems.

**Enzymatic fragmentation reagents included.

References

1. Allgäuer, M.; Budczies, J.; Christopoulos, P.; Endris, V.; Lier, A.; Rempel, E.; Volckmar, A.-L.; Kirchner, M.; von Winterfeld, M.; Leichsenring, J.; Neumann, O.; Fröhling, S.; Penzel, R.; Thomas, M.; Schirmacher, P.; Stenzinger, A. Implementing Tumor Mutational Burden (TMB) Analysis in Routine Diagnostics - A Primer for Molecular Pathologists and Clinicians. *Transl. Lung Cancer Res.* **2018**, 7 (6), 703-715. DOI: 10.21037/tlcr.2018.08.14.

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