

SureSelect Community Design Glasgow Cancer Panels

Biomarkers with proven or emerging utility in predicting outcome and/or drug response/resistance - **The clinical space**

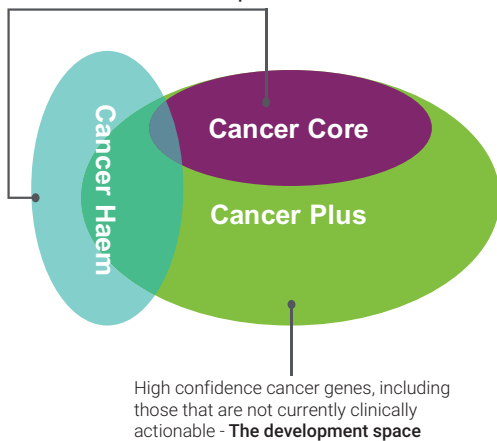


Figure 1. Illustration of the GPOL cancer assay suite of panels that are commercially available as part of Agilent's Community Designs. We currently offer the SureSelect Community Design (CD) Cancer Core, Cancer Plus, and Cancer Haem panels. This figure illustrates the relative size and content overlap of each panel.

Genomics is a key element in precision medicine's potential to transform oncology. Hybrid capture-based, targeted next-generation sequencing (NGS) represents a particularly promising technology as it enables the focused profiling of each of the many cancer-relevant loci. This approach allows for rapid and cost-effective detection of most cancer-relevant genomic events, with the added advantage of FFPE tissue sample compatibility.

The Glasgow Precision Oncology Laboratory (GPOL) is a team of scientists with internationally recognized expertise in the technology, biology, and clinical utility of cancer genomics. Among their achievements is their detailed curation of genomic data to define the landscape of clinically and biologically significant genomic events in cancer. This includes not only a published literature review (see references 1-3), but also the International Cancer Genome Consortium (ICGC) and the Pan-Cancer Analysis of Whole Genomes (PCAWG) study.

The GPOL has leveraged these insights to design the hybrid capture-based SureSelect cancer NGS panels. With the SureSelect platform, the GPOL team has developed a suite of affordable, fit-for-purpose cancer genomic assays for both solid and haematological cancers (Figure 1). These assays have been developed specifically to address the challenges of real-world oncology. This includes both current and emerging routine healthcare, therapeutic development (including participant selection for clinical trials) and discovering markers of resistance and treatment response. With the high-quality data produced by the SureSelect platform, delivered by its fast and automatable workflow, the GPOL is leading the implementation of broad genomic testing.

The SureSelect CD Glasgow Cancer Core Panel

The Glasgow Cancer Core Panel is designed for the comprehensive profiling of genomic events in solid tumors at a cost that is suitable for the healthcare system. These genomic events are linked with response or resistance to specific therapies, including approved agents and drugs in clinical development. This panel assays 174 genes for events including single nucleotide variants (SNVs), copy number variants (CNVs), short insertion and deletions (indels), large structural variants, and gene fusions/rearrangements (Table 1). This panel is suitable for characterizing cancer biomarkers with proven or emerging clinical utilities.

Note: NTRK fusions create oncogenic proteins and there is increasing evidence that TRK inhibitors can be used in the treatment of cancer⁴. NTRK1 and ETV6, the most common fusion partner genes of NTRK3, are covered by this panel for gene rearrangement.

Table 1. The genes and associated variant types covered in the SureSelect CD Glasgow Cancer Core Panel.

AKT1	•◆	CTNNB1	•◆	KIT	•◆	POLE	•
AKT2	•◆	DAXX	•	KLF4	•	POLQ	•
AKT3	•◆	DICER1	•	KMT2A	•	PPP2R1A	•
ALK	•◆*	DNMT3A	•	KRAS	•◆	PTCH1	•
AMER1	•	EGFR	•◆*	MAP2K1	•	PTEN	◆+
APC	•◆	EP300	•	MAP2K2	•■	PTPN11	•
APLN	•◆+	EPHA3	•◆	MAP2K4	•	RAC1	•
AR	•◆	ERBB2	•◆	MAP3K1	•	RAD21	•
ARAF	•	ERBB3	•	MAPK1	•	RAD50	•
ARID1A	•◆	ERBB4	•	MAX	•	RAF1	•◆*
ARID1B	•	ERG	◆*	MCL1	◆	RB1	◆+
ARID2	•	ESR1	•◆	MDM2	◆	RET	•◆*
ASXL1	•	ETV6	•◆*	MED12	•	RHOA	•
ATM	•◆	EZH2	•◆	MEN1	•	RNF43	•◆
ATR	•	FAS	•	MET	•◆	ROS1	•*
ATRX	•	FBXW7	•	MLH1	•◆	RPL5	•
AURKA	◆	FGF19	◆	MSH2	•	RUNX1	•
AXL	◆	FGFR1	•◆	MSH6	•	SETBP1	•
B2M	◆+	FGFR2	•◆	MTOR	•	SETD2	•
BAP1	•	FGFR3	•◆	MUTYH	•	SF3B1	•
BCL2	◆	FGFR4	•◆	MYB	•	SMAD4	•◆
BLM	•	GATA3	•	MYC	•◆	SMARCA4	•
BRAF	•◆*	GNA11	•	MYCN	•	SMARCB1	•
BRCA1	◆+	GNAQ	•	NBN	•	SMO	•
BRCA2	◆+	GNAS	•	NF1	•◆	SOCS1	•◆
CBL	•	H3F3A	•	NF2	•	SPOP	•
CCND1	•◆	H3F3B	•	NFE2L2	•◆	SRC	◆
CCND2	◆	HGF	◆	NOTCH1	•◆	STAG1	•
CCND3	•◆	HIST1H3B	•	NOTCH2	•◆	STAG2	•
CCNE1	◆	HIST1H3C	•	NOTCH3	•◆	STAT3	•◆
CD274	•◆*	HIST2H3C	•	NOTCH4	•◆	STAT5B	•
CD58	•◆	HLA-A	◆+	NPM1	•	STK11	•◆
CDK12	•	HLA-B	◆+	NRAS	•	SYK	•◆
CDK2	◆	HLA-C	◆+	NTRK1	•◆*	TERT	◆*■
CDK4	•◆	HNF1A	•	PALB2	•◆	TGFBR2	•
CDK6	◆	HRAS	•	PBRM1	•	TP53	◆+
CDKN1A	•	IDH1	•	PDCD1LG2	•◆	TSC1	◆+
CDKN1B	•◆	IDH2	•	PDGFRA	•◆	TSC2	•◆
CDKN2A	◆+	IGF1R	◆	PDGFRB	•◆	U2AF1	•
CDKN2B	◆+	JAK1	•◆	PHF6	•	VHL	•
CHEK2	•	JAK2	•◆	PIK3CA	•	WT1	•◆
CIITA	•◆	JAK3	•◆	PIK3CB	•◆	YAP1	◆
CREBBP	•	JUN	◆	PIK3R1	•		
CTCF	•	KDR	•	PMS2	•		

Targeted variant types:

• coding exons ◆ copy number * rearrangement ■ regulatory region + full footprint

The SureSelect CD Glasgow Cancer Plus Panel

The Glasgow Cancer Plus Panel targets a total of 353 cancer genes: the 174 genes covered in the Cancer Core Panel and an additional 179 high-confidence cancer genes. The latter genes represent candidates that are not yet clinically actionable but are aimed towards hypothesis-driven translational research or biomarker development for clinical trials and/or studies. The Cancer Plus panel is being used in ongoing clinical trials, including Scotland's IMAGINE trial, which generates genomic profiles for patients in phase I clinical trials.

Table 2. The genes and associated variant types covered by the SureSelect CD Glasgow Cancer Plus Panel, in addition to those covered in the Core Panel.

ABL1	•◆	EIF4A2	•◆	MDM4	•◆	RFXAP	•◆
ABL2	•◆	ELF3	•◆	MECOM	•◆	RHEB	•◆
ABR	•◆	ELOC	•◆	MGA	•◆	RICTOR	•◆
ABRAXAS1	•◆	EPHA2	•◆	MGMT	•◆	RIT1	•◆
ACVR1B	•◆	ERCC2	•◆	MRE11	•◆	RPL22	•◆
ACVR2A	•◆	ERCC3	•◆	MSH3	•◆	SERPINB3	•◆
AJUBA	•◆	ERCC4	•◆	MYCL	•◆	SERPINB4	•◆
AKAP9	•◆	ERCC5	•◆	MYH9	•◆	SLC34A2	*◆
ALOX12B	•◆	ETV1	•◆	NAB2	*◆	SMAD2	•◆
ALOX15B	•◆	ETV4	•◆	NCOA2	•◆	SMAD3	•◆
ARHGAP35	•◆	ETV5	•◆	NCOR1	•	SMC1A	•◆
ARID5B	•◆	FANCA	•◆	NLRC5	•◆	SMC3	•◆
ASXL2	•◆	FANCC	•◆	NRG1	•◆*	SMG1	•◆
AURKB	•◆	FANCD2	•◆	NSD1	•◆	SOS1	•◆
AURKC	•◆	FANCE	•◆	NSD3	•◆	SOX17	•◆
AXIN1	•◆	FANCF	•◆	NTRK2	•◆	SOX9	•◆
AXIN2	•◆	FANCG	•◆	NTRK3	•◆	SPEN	•◆
BARD1	•◆	FANCL	•◆	PARP1	•◆	SRSF2	•◆
BCOR	•◆	FANCM	•◆	PAX5	•◆	STAT1	•◆
BIRC3	•◆	FAT1	•◆	PCBP1	•◆	TAF1	•◆
BRIP1	•◆	FLT1	•◆	PIAS3	•◆	TAF3	•◆
CARD11	•◆	FOXA1	•◆*	PIAS4	•◆	TAP1	•◆
CASP8	•◆	FOXA2	•◆	PIK3CD	•◆	TAP2	•◆
CBFB	•◆	FOXL2	•◆	PIK3R2	•◆	TAPBP	•◆
CD74	*◆	FOXO1	•◆	PIM1	•◆	TBL1XR1	•◆
CDC73	•◆	FOXP1	•◆	PLCG1	•◆	TBX3	•◆
CDH1	•◆	FUBP1	•◆	PMS1	•◆	TCF12	•◆
CDK8	•◆	GATA6	•◆	POLQ	•	TCF7L2	•◆
CDKN1C	•◆	GNA13	•◆	PPM1D	•◆	TET2	•◆
CDKN2C	•◆	GPS2	•◆	PPP2R2A	•◆	TGFBRN	•◆
CHD4	•◆	HIF1A	•◆	PPP4R2	•◆	TMPRSS2	•◆
CHD8	•◆	HIST1H1C	•◆	PPP6C	•◆	TP53BP1	•◆
CHEK1	•◆	IDO1	•◆	PRKAR1A	•◆	TP73	•◆
CIC	•◆	IDO2	•◆	PSIP1	•◆	TRAF7	•◆
CKS1B	•◆	IFNGR1	•◆	PTK2	•◆	UVRAG	•◆
CTLA4	•◆	IFNGR2	•◆	PTPRD	•◆	WRN	•◆
CUL3	•◆	IL6ST	•◆	QSER1	•◆	XBP1	•◆
CUX1	•◆	IRF1	•◆	RAD51B	•◆	XPO1	•◆
CYLD	•◆	KDM5C	•◆	RAD51C	•◆	ZFH3	•◆
DDR2	•◆	KDM6A	•◆	RAD51D	•◆	ZFP36L1	•◆
DDX3X	•◆	KEAP1	•◆	RAD52	•◆	ZMYM2	•◆
DDX5	•◆	KMT2B	•◆	RAD54L	•◆	ZMYM3	•◆
DEFB134	•◆	KMT2C	•◆	RASA1	•◆	ZNF703	•◆
DHX9	•◆	KMT2D	•◆	RBM10	•◆	ZNF750	•◆
DNMT3A	•	LZTR1	•◆	RFX5	•◆		

Targeted variant types:

• coding exons ◆ copy number * rearrangement

The SureSelect CD Glasgow Cancer Haem Panel

The Glasgow Cancer Haem Panel covers 262 genes that are clinically relevant for hematological cancers. This panel possesses a probe backbone to aid CNV characterization in addition to detecting SNVs and indels. It also interrogates microsatellite sites for microsatellite instability (MSI) status and offers sufficient panel size to call Tumor Mutation Burden (TMB).

Table 3. The genes and associated variant types covered by the Glasgow Cancer Haem Panel.

ABL1	●	CALR	●◆	CNOT3	●
ACD	●	CARD11	●	CRBN	●
AKT1	●	CASP8	●	CREBBP	●◆
ALK	●	CBFB	●	CSF1R	●
ANKRD26	●■	CBL	●◆	CSF3R	●
ARAF	●	CCND1	●◆	CTCF	●
ARID1A	●	CCND2	◆	CTNNB1	●
ARID1B	●	CCND3	●◆	CUX1	●◆
ARID2	●	CCNE1	◆	CXCR4	●
ASXL1	●+	CCR6	●	CYLD	●
ASXL2	●	CD22	●	DDX3X	●
ATM	●	CD274	◆■	DDX41	●
ATRX	●	CD28	●	DIS3	●
B2M	●+	CD58	●+	DNMT3A	●
BCL10	●	CD70	●	DTX1	●
BCL11A	◆	CD79A	●	EBF1	●◆
BCL2	●◆*	CD79B	●	EGFR	●
BCL6	●*	CD83	●	EGR1	●
BCL7A	●	CDK4	●◆	EGR2	●◆
BCOR	●	CDK6	◆	ELANE	●
BCORL1	●	CDKN1B	●	EP300	●
BIRC2	●	CDKN2A	●+	ERBB2	●◆
BIRC3	●	CDKN2B	●+	ERBB3	●
BLM	●	CDKN2C	●	ETNK1	●
BRAF	●	CEBPA	●◆	ETV6	●◆*
BTG1	●◆	CHEK2	●	EZH2	●◆
BTG2	●	CIITA	●+	FAS	●
BTK	●	CKS1B	◆	FAT1	●

FAT3	●	ITPKB	●	NTRK1	●◆*	SF3B1	●
FAT4	●	JAK1	●	P2RY8	●	SGK1	●
FBXO11	●	JAK2	●◆	PAX5	●◆	SH2B3	●
FBXW7	●	JAK3	●	PDCD1LG2	◆	SMARCA4	●
FGFR1	●◆	KDM6A	●	PDGFRA	●	SMARCB1	●
FGFR2	●◆	KIT	●	PDGFRB	●	SMC1A	●
FGFR3	●◆	KLF2	●	PDS5B	●	SMC3	●
FLT3	●◆*	KLHL6	●	PHF6	●	SOCS1	●
FOXO1	●	KMT2A	●◆*	PIGA	●	SPEN	●
GATA1	●	KMT2C	●	PIK3CA	●	SPIB	●◆
GATA2	●	KMT2D	●◆	PIK3CB	●◆	SRC	◆
GATA3	●	KRAS	●	PIK3CD	●	SRSF2	●
GNA13	●	LCK	●	KIK3R1	●	STAG2	●
GNAS	●	LMO2	■	PIM1	●	STAT3	●
GPR34	●	LTB	●	PLCG2	●	STAT5B	●
GTF2I	●	MAP2K1	●	POT1	●	STAT6	●
HIST1H1B	●	MAP2K4	●	POU2AF1	●	STK11	●
HIST1H1C	●	MAP3K1	●	POU2F2	●	SUZ12	●
HIST1H1D	●	MCL1	◆	PPM1D	●	SYK	●
HIST1H1E	●	MECOM	●	PRDM1	●◆	TBL1XR1	●
HIST1H2AC	●	MED12	●	PRKCB	●	TCF3	●
HIST1H2AG	●	MEF2B	●	PRPF8	●	TENT5C	●
HIST1H2AM	●	MET	◆	PTCH1	●	TERC	●
HIST1H2BC	●	MGA	●	PTEN	●+	TERT	●◆*
HIST1H2BD	●	MPEG1	●	PTPN11	●	TET2	●◆
HIST1H2BG	●	MPL	●	PTPN2	●	THRAP3	●
HIST1H2BK	●	MSH2	●	PTPN6	●	TLR2	●
HIST1H3B	●	MSH6	●	PTPRC	●	TMEM30A	●
HIST1H3G	●	MTOR	●	PTPRD	●	TMSB4X	●
HLA-A	●+	MYB	●◆	RAD21	●	TNF	●
HLA-B	●+	MYC	●◆*	RAD51	●	TNFAIP2	◆
HLA-C	●+	MYD88	●	RASA2	●	TNFAIP3	●◆
HRAS	●	NF1	●◆	RB1	●◆	TNFRSF14	●◆
ID3	●	NF2	●	RCOR1	◆	TP53	●+
IDH1	●	NFE2	●	REL	◆	TRAF3	●◆
IDH2	●	NFKB1	●	RHOA	●	U2AF1	●
IGH	●*	NFKB2	●	ROS1	●	U2AF2	●
IKKB	●	NFKBIA	●	RPS15	●	UBR5	●
IKZF1	●+	NFKBIE	●	RUNX1	●◆	VAV1	●
IKZF3	●	NFKBIZ	●◆	SAMD9	●	WT1	●+
IL2RG	●	NOTCH1	●	SAMD9L	●	XPO1	●
IL7R	●	NOTCH2	●	SETBP1	●	ZFP36L1	●
IRF1	●	NPM1	●	SETD2	●	ZRSR2	●
IRF4	●	NRAS	●	SETDB1	●		
IRF8	●	NSD2	●	SF1	●		

Targeted variant types:

● coding exons ◆ copy number * rearrangement ■ regulatory region + full footprint

Features of all Glasgow Cancer panels

All Glasgow cancer panels have been designed with a plethora of additional features to aid their clinical utility (subject to the proper analysis). These features include a footprint of the appropriate size for tumour mutation burden (TMB) measurement and markers for microsatellite instability (MSI) evaluation. Additionally, the panels offer tools for examining the immunological status of a sample (e.g., HLA typing and levels of retrotransposon activity). These panels can also inform your workflow by including content for sample genotyping and assaying for pre-receipt sample contamination.

Table 4. Comparison of the features of the Glasgow cancer panels.

Panel	Utility	NO. of Genes	Assay footprint	Designed for TMB & MSI	Compatible sample types*	Sequencing requirement
Cancer Core	Comprehensive profiling of actionable genomic events in solid tumors at a cost suitable for the healthcare system.	174	1.87 Mb	Yes	Genomic DNA derived from: - Fresh frozen tissue/cells - FFPE tissues - Blood - Plasma	32 samples on one NextSeq High Output run
Cancer Plus	A larger panel to channel patients towards appropriate clinical trials or for use in the translational research space.	353	3.96 Mb	Yes		16 samples on one NextSeq High Output run
Cancer Haem	Specifically designed to target genes relevant to haematological malignancies.	262	2.13 Mb	Yes		24 to 32 samples on one NextSeq High Output run

*When coupled with SureSelect XT Low Input, XT HS or XT HS2 library preparation.

The Glasgow cancer panels are supported by Agilent's streamlined and automated NGS workflow

All Glasgow cancer panels are compatible with our SureSelect XT HS1/Low Input and XT HS2 library preparation and target enrichment solutions for efficient and streamlined NGS workflows. These solutions are optimized for low input (as little as 10 ng of intact or FFPE DNA), making them an ideal choice for both solid tumor and hematological samples.

The Glasgow cancer panels are also compatible with our new Magnis NGS Library Prep system, a fully automated instrument that delivers highly reproducible results. This bench-top instrument requires minimal expertise and allows assays to be set up in <5 minutes with pre-aliquoted reagents and pre-set protocols. Combining Glasgow Cancer panels with the Magnis has enabled a 72-hour turnaround time from sample to reported result (Figure 2), offering rapid and reproducible results, even from difficult sample types.

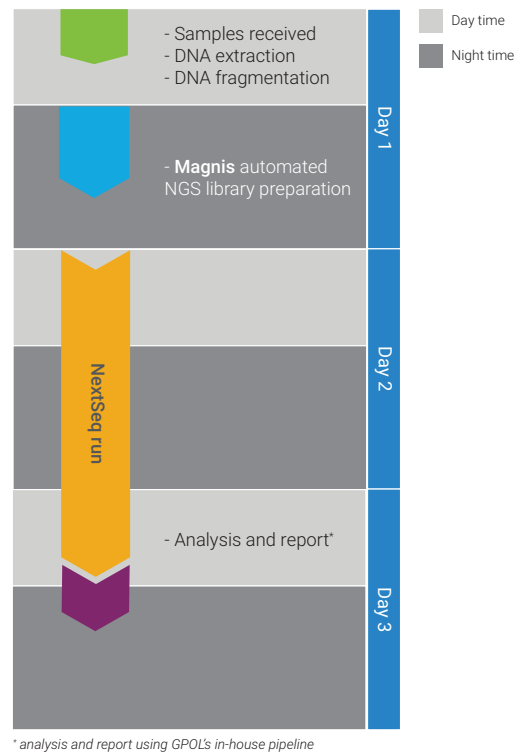


Figure 2. The workflow of the Glasgow cancer assays powered by the Magnis NGS Library Prep system enables delivery of comprehensive cancer genomic insights from FFPE samples in only 72 hours.

Agilent Community Design Program

Created with internationally recognized knowledge in cancer genomics, the Glasgow cancer panels are now commercially available through the Agilent Community Design Program (ACD) (Table 5).

The ACD offers NGS panels designed by, or in collaboration with, experts in various research fields. These panels, which are priced significantly lower than custom-made panels of equivalent sizes, are made to order and ship in two weeks.

Agilent has not validated the performance of the panels in the Agilent Community Design Program.

Table 5. Ordering information of the SureSelect Community Design GLasgow cancerp panels. These part numbers cover the capture probe library only. Library prep and target enrichment kits must be purchased separately.

Part Number	Product Description
5191-6736	SureSelect CD Glasgow Cancer Core Panel, 16 rxn
5191-6737	SureSelect CD Glasgow Cancer Core Panel, 96 rxn
5191-6738	SureSelect CD Glasgow Cancer Core Panel, 96 rxn, Automation
5191-6740	SureSelect CD Glasgow Cancer Core Panel, Pre-capture Pooling, 96 rxn
5191-6741	SureSelect CD Glasgow Cancer Core Panel, Pre-capture Pooling, 96 rxn, Automation
5191-6950	SureSelect CD Glasgow Cancer Plus Panel, 16 rxn
5191-6951	SureSelect CD Glasgow Cancer Plus Panel, 96 rxn
5191-6952	SureSelect CD Glasgow Cancer Plus Panel, 96 rxn, Automation
5191-6953	SureSelect CD Glasgow Cancer Plus Panel, Pre-capture Pooling, 96 rxn
5191-6954	SureSelect CD Glasgow Cancer Plus Panel, Pre-capture Pooling, 96 rxn, Automation
5191-6955	SureSelect CD Glasgow Cancer Haem Panel, 16 rxn
5191-6956	SureSelect CD Glasgow Cancer Haem Panel, 96 rxn
5191-6957	SureSelect CD Glasgow Cancer Haem Panel, 96 rxn, Automation
5191-6958	SureSelect CD Glasgow Cancer Haem Panel, Pre-capture Pooling, 96 rxn
5191-6959	SureSelect CD Glasgow Cancer Haem Panel, Pre-capture Pooling, 96 rxn, Automation

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References - Key literature used in panel design

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4. Larotrectinib for treating NTRK fusion-positive solid tumours. <https://www.nice.org.uk/guidance/TA630>

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