PGD | CANCER*SELECT*-R™ 203

CANCER*SELECT*-R™ 203 APPROACH

PGDx has developed proprietary techniques for analysis of cancer genomes, including methods for extracting genetic material from frozen or fixed tumor samples, high-throughput next-generation sequencing (NGS), patented approaches for novel genetic analyses, and proprietary data analysis algorithms.

Cancer*Select*-R™ analyzes the regions of a targeted panel of 203 well-characterized cancer genes. Both tumor and normal samples are requested and analyzed using proprietary methods that accommodate low abundance, poor quality sample DNA. Combined with a proprietary capture design and high coverage next-generation sequencing, tumor-specific (somatic) mutations, copy number changes and translocations are identified with a high sensitivity and specificity.

CANCER*SELECT*-R™ 203 HIGHLIGHTS

- Detailed visual inspection and curation of tumor-specific mutations by world-class cancer bioinformatic experts
- DNA extraction methods that accommodate poor quality and low cellularity tumor samples
- Proprietary analysis algorithms to identify bona-fide sequence changes and to exclude sequence artifacts
- Identification of mutated genes with biologic or clinical implications in human cancer
- Proprietary capture design and patented Digital Karyotyping analysis for high resolution annotation of copy number alterations with high sensitivity and specificity
- CHASM analysis algorithms to evaluate mutation properties and importance of non-hotspot mutations
- PARE (Personalized Analysis of Rearranged Ends) technology to identify structural changes in tumor-specific DNA, including translocations

CANCER*SELECT*-R™ 203 ANALYSIS DELIVERABLES

- Comprehensive pathological evaluation of tumor sample
- Tumor-specific sequence alterations (single base and small indel alterations)
- Tumor-specific copy number alterations and translocations
- Functional impact of mutations (predicted protein alterations and domain consequences)
- Mutated genes and pathways with biological or clinical implications
- In-depth COSMIC analysis for recurrent mutations across tumor types
- CHASM analysis for identification of driver mutations
- Data summary statistics (read data and depth distribution across target regions)
- Integrated Analysis Report (incidences and frequencies of mutations identified)

CANCER*SELECT*-R™ 203 SEQUENCING DELIVERABLES & ANALYSES

Analysis Metrics	Cancer*Select*-R™ 203
Regions Analyzed	203 genes
Sample Prep and NGS Sequencing	✓
Sequence Mapping	✓
Somatic Mutation Analysis	✓
Copy Number Analysis	✓
Structural Alteration Analysis	✓
Germline Variant Analysis	✓
Pathway and Functional Analysis	✓
Integrated Project Analyses	✓
Microsatellite Instability Analysis	✓

*Germline variant analysis is optional

CANCER*SELECT*-R™ 203 SEQUENCING KEY METRICS

Regions Analyzed	Coding regions of 195 genes and selected regions of 24 genes
Sequencing Method	Illumina next generation sequencing
Bioinformatics	Proprietary methods and visual inspection
Assay Sensitivity	>99%
Assay Specificity	>99.99%
Sequencing Coverage	1,500x
Turn-around Time	4 weeks (rush available)
Sample Requirements	Tumor only or tumor and matched normal (optimal results)
Sample Types	Frozen tumor, FFPE, cell lines, blood, saliva, and xenograft
DNA Input Required	1 µg (minimum 50 ng)

Related References

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GENES EVALUATED IN CANCER*SELECT*-R™ 203

Rearrangement analyses for selected regions of 24 well-characterized cancer genes.

ALK	EGFR	EWSR1	PDGFRA	RET
BCL2	ETV1	FGFR3	PDGFRB	ROS1
BCR	ETV4	MLL	PRKACA	TACC3
BRAF	ETV5	MYC	RAF1	TMPRSS2
DNAJB1	ETV6	NTRK1	RARA	

Sequence and copy number analyses (*) for the coding regions of 195 well-characterized cancer genes.

ABL1*	CIC	FGFR2*	MPL*	RAD51C
ACVR1	CREBBP	FGFR3*	MSH2	RAF1
AKT1*	CSF1R*	FGFR4*	MSH6	RB1
AKT2*	CTNNB1*	FH	MTOR	RECQL4
ALK*	CYLD	FLCN	MUTYH	RET*
APC	DAXX	FLT3*	MYC*	RNF43
AR*	DDB2	FLT4	MYCL1*	ROS1
ARID1A	DDR2	FOXL2*	MYCN*	RUNX1*
ARID1B	DICER1	GATA1	MYD88*	SBDS
ASXL1	DNMT3A*	GATA2*	NBN	SDHAF2
ATM	EGFR*	GNA11*	NCOA3*	SDHB
ATRX	EP300	GNAQ*	NF1	SDHC
AURKA	ERBB2*	GNAS*	NF2	SDHD
AXIN2	ERBB3*	GPC3	NKX2-1*	SF3B1*
BAP1	ERBB4*	H3F3A*	NOTCH1*	SMAD2
BCL2*	ERCC1	H3F3B	NOTCH2*	SMAD3
BCR	ERCC2	HNF1A	NOTCH3*	SMAD4
BLM	ERCC3	HRAS*	NOTCH4*	SMARCB1
BMPR1A	ERCC4	IDH1*	NPM1	SMO*
BRAF*	ERCC5	IDH2*	NRAS*	SRC
BRCA1	ESR1	IGF1R*	NTRK1	STAG2
BRCA2	ETV1	IGF2R*	PALB2	STK11
BRIP1	ETV5	IKZF1	PAX5*	SUFU
BTK	EWSR1	JAK1*	PBRM1	TERT
BUB1B	EXT1	JAK2*	PDGFRA*	TET2
CALR	EXT2	JAK3*	PHOX2B	TGFBR2
CBL*	EZH2*	KDR*	PIK3CA*	TNFAIP3
CCND1*	FANCA	KIT*	PIK3R1	TOP1
CCNE1*	FANCB	KRAS*	PMS1	TP53
CDC73	FANCC	MAML1*	PMS2	TSC1
CDH1	FANCD2	MAP2K1*	POLD1	TSC2
CDK4*	FANCE	MAP2K4	POLE	TSHR*
CDK6*	FANCF	MDM2*	POLH	VHL
CDKN1B	FANCG	MDM4*	POT1	WAS
CDKN2A	FANCI	MED12*	PRKAR1A	WRN
CDKN2B	FANCL	MEN1	PRSS1	WT1
CDKN2C	FANCM	MET*	PTCH1	XPA
CEBPA	FBXW7	MLH1	PTEN	XPC
CHEK2	FGFR1	MLL*	PTPN11*	XRCC1

Microsatellite instability analyses for 5 markers

BAT-25	BAT-26	MONO-27	NR-21	NR-24

FIGURE 1. DEPICTION OF NEXT GENERATION SEQUENCING DATA FOR IDENTIFICATION OF TRANSLOCATIONS