PGD | CANCER*SELECT*-R™ 88

CANCER*SELECT*-R™ 88 APPROACH

PGDx has developed proprietary techniques 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 88 well-characterized cancer genes. Both tumor and normal samples are requested and prepared 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™ 88 HIGHLIGHTS

- Detailed visual inspection and curation of tumor-specific mutations by world-class cancer bioinformatic experts
- Proprietary 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 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

COMPREHENSIVE CANCER*SELECT*-R™ 88 ANALYSIS DELIVERABLES

- 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™ 88 SEQUENCING DELIVERABLES & ANALYSES

Analysis Metrics	Cancer*Select*-R™ 88
Regions Analyzed	Coding regions of 76 genes and selected regions of 14 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™ 88 SEQUENCING KEY METRICS

Regions Analyzed	Selected regions of 88 genes
Sequencing Method	Illumina next generation sequencing
Bioinformatics	Proprietary analysis methods supplemented by visual inspection
Assay Sensitivity	>99%
Assay Specificity	>99.99%
Sequencing Coverage	1,000x
Turn-around Time	3 weeks
Sample Requirements	Tumor only or tumor and matched normal*
Sample Types	Frozen tumor, FFPE, cell lines, blood, saliva, and xenograft
DNA Input Required	1 µg (minimum 50 ng)

*For maximum ability to differentiate somatic mutations from germline mutations, tumor and matched normal samples are recommended.

Related References
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GENES EVALUATED IN CANCER*SELECT*-R™ 88

Sequence analyses for 76 well-characterized cancer genes

ABL1	ERBB4	GNAQ	MTOR	RET
AKT1	EZH2	GNAS	NF1	ROS1
ALK	FANCA	HNF1A	NF2	SMAD4
APC	FANCC	HRAS	NOTCH1	SMARCB1
ATM	FANCD2	IDH1	NPM1	SMO
BRAF	FANCE	IDH2	NRAS	SRC
BRCA1	FANCF	JAK2	NTRK1	STK11
BRCA2	FANCG	JAK3	PALB2	TERT
BRIP1	FANCL	KDR	PDGFRA	TP53
CDH1	FBXW7	KIT	PDGFRB	TSC1
CDKN2A	FGFR1	KRAS	PIK3CA	TSC2
CSF1R	FGFR2	MET	PMS2	VHL
CTNNB1	FGFR3	MLH1	PTCH1	
DDR2	FLT3	MPL	PTEN	
EGFR	FOXL2	MSH2	PTPN11	
ERBB2	GNA11	MSH6	RB1	

Copy number analyses for 13 well-characterized cancer genes

ALK	ERBB3	FGFR3	MYC	RET
EGFR	FGFR1	KIT	MYCN	
ERBB2	FGFR2	MET	PDGFRA	

Rearrangement analyses for 14 well-characterized cancer genes

ALK	EGFR	ETV6	PDGFRA	ROS1
BCL2	ETV1	EWSR1	PDGFRB	TMPRSS2
BCR	ETV4	MLL	RARA	

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