

TECHNICAL INFORMATION

A Comprehensive Genomic Profiling Test for Cancer

TESTING COMPONENTS

PCDx is a comprehensive genomic profiling test (CGP) test that has been designed to analyze the most clinically actionable genomic variations in cancer, including mutations, copy number variations, fusions, mRNA expression and protein expression by IHC, providing clinicians with a useful genomic and proteomic blueprint of a patient's cancer. Paradigm's proprietary multiplexed sequencing analysis enables these analyses to be performed with the fastest available turnaround time and an exceptional level of accuracy on a very limited amount of tissue in a CLIA-Certified laboratory. At a typical median depth of coverage >5,000x, the PCDx test was developed to provide clinical grade sequencing results, ensuring the highest level of confidence that both our positive and negative calls are correct.

Turn-Around Time (TAT)	4-5 Business Days
Sample Requirements	≥4% tumor content, 6-10 10 μm thick curls or an FFPE block, needle biopsies acceptable
Potential Unique Therapies Reported	83 + 12 Combination Therapies
Genes Tested by Next-Generation Sequencing	137 genes
Alterations Tested by NGS	Mutations, Copy Number Alterations, Fusions, mRNA
Typical Median Depth of Coverage	>5,000x
Protein Targets Analyzed	up to 24
Clinical Trials Matching	Yes

CLINICALLY VALIDATED IMPROVEMENT IN PROGRESSION FREE SURVIVAL

Paradigm's testing was independently validated through a prospective clinical analysis and published by a team of leading independent oncologists and researchers at the Indiana University School of Medicine showing that the progression free survival interval increased by 43% when treatment was based on Paradigm's test results.

¹Radovich, M., et al. (2016). Clinical benefit of a precision medicine based approach for guiding treatment of refractory cancers. *Oncotarget*, 7(35), 56491–56500.

RAPID RESULTS ON LIMITED TISSUE SPECIMENS

Paradigm understands that obtaining an adequate amount of quality tissue for molecular analysis can be a challenge. Paradigm excels at providing robust analysis and results on extremely small tissue specimens.

Compared to the sample failure rates of other leading NGS solutions which was recently published to be 18%, Paradigm's sample success rate is 94% and continues to improve. This is based on the first 2,900 patients run on the PCDx platform where only 175 patients had insufficient tissue for analysis. Essentially, specimens rejected by quantity not sufficient (QNS) is three times more likely to occur at the leading provider than for testing at Paradigm. Paradigm consistently gets comprehensive and accurate results off of fine needle aspirates down to 4% tumor. ²

CLINICAL REPORT

Each PCDx report provides an individualized genomic landscape, which summarizes the key genomic alterations identified through the testing process. The report is designed to identify and then summarize all potentially actionable classes of alterations in key cancer-related genes with their respective drug associations and potential clinical trials.

EVIDENCE PROCESS

Paradigm's team and network of leading oncologists, scientists, and physicians continuously monitor updates to the medical literature to ensure that the PCDx test is up to date. This includes evaluating the latest peer reviewed literature to ensure PCDx associations facilitate better personalized medicine.

SUMMARY

With clinical-grade accuracy & quality at >5,000x coverage and rapid turnaround time, PCDx delivers a comprehensive NGS solution that allows critical genomic information to be utilized by physicians to inform treatment decisions for patients being treated for complex and difficult to treat cancers. The PCDx report offers comprehensive, relevant and actionable findings, highlighting the underlying mechanisms of the patient's individual tumor. These findings are associated with specific drugs or clinical trials that may provide critical information for the patients next-step in treatment.

²Kalyan C. Mantripragada, et al., *Clinical Trial Accrual Targeting Genomic Alterations After Next-Generation Sequencing at a Non-National Cancer Institute-Designated Cancer Program*. *Journal of Oncology Practice* (2016) 12:4, e396-e404.



PARADIGM PCDx GENE LIST

DNA MUTATION		COPY NUMBER VARIATION	mRNA EXPRESSION		PROTEIN EXPRESSION BY IHC	FUSIONS (IF IHC POSITIVE)
AKT1	MAP2K1	19Q	AR	KIT	ALK	NTRK1
ALK	MAP2K2	1P	AREG	LRP6	AR	NTRK2
BRAF	MAP3K1	ALK	ARID1A	MET	CAIX	NTRK3
BRCA1	MET	AURKA	BAD	MGMT	ER	RET
BRCA2	MSH6	C11ORF30	BAX	MITF	HENT1	ROS1
CREBBP	MSI*	CCND1	BCL2	MTOR	HER2	
CSF1R	MTOR	CCND2	BIRC5	NFKB1	IDO	
DDR2	NRAS	CCND3	BRCA1	PARP1	MET	
EGFR	PDGFRA	CCNE1	CA9	PDGFRB	MGMT	
EP300	PIK3CA	CDK4	CDA	PGR	PD1	
ERBB2	PTCH1	CDK6	CDH1	PTEN	PDL1	
ERBB4	ROS1	CDKN2A	CES2	PTGS2	PR	
ERCC2	SMO	EGFR	CHUK	PTPN6	PTEN	
ERRF1	TGFBR2	ERBB2	DCK	RELA	RET	
ESR1	TP53	FGF3	DHFR	RPS6KB1	ROS1	
FGFR2	TSC1	FGF4	DPYD	RRM1	TOPO1	
FGFR3	TSC2	FGFR1	EPHA2	SLC29A1	TP	
FLT3		FGFR2	ERBB2	SSTR2	TRKpan	
GATA3		FGFR3	ERBB3	TNFSF13	TS	
GNAQ		MET	ERCC1	TOP2A	TUBB3	
GNAS		MYC	EREG	TUBB3	MLH1	
HRAS		MYCN	ESR1	TYMP	MSH2	
IDH1		NTRK1	EZH2	TYMS	MSH6	
IDH2		SMAD4	FGFR1	VEGFA	PMS2	
KIT		TOP2A	IGF1R			
KRAS		VEGFA	KDR			

*If requested by physician.

DRUGS ASSOCIATED

PCDx biomarker analysis associates with a wide range of cancer therapies. Select drugs associated with PCDx include:

Abiraterone	Ceritinib	Everolimus	Liposomal	Oxaliplatin	Sunitinib
Ado-trastuzumab	Cetuximab	Exemestane	Doxorubicin	Paclitaxel	Tamoxifen
emtansine	Cisplatin	Fluorouracil	Medroxy-progesterone	Palbociclib	Temozolomide
Afatinib	Crizotinib	Flutamide	Methotrexate	Panitumumab	Temsirolimus
Alectinib	Dabrafenib	Fulvestrant	Mitomycin	Pazopanib	Topotecan
Anastrozole	Dasatinib	Gefitinib	Mitotane	Pembrolizumab	Toremifene
Atezolizumab	Dinutuximab	Gemcitabine	Neratinib	Pemetrexed	Trabectedin
Avelumab	Docetaxel	Idelalisib	Nilotinib	Pertuzumab	Trametinib
Bevacizumab	Doxorubicin	Imatinib	Niraparib	Procarbazine	Trastuzumab
Bicalutamide	Durvalumab	Interleukin-2	Nivolumab	Regorafenib	Vemurafenib
Brigatinib	Enzalutamide	Ipilimumab	Octreotide	Ribociclib	Vendetanib
Cabozantinib	Epirubicin	Irinotecan	Olaparib	Rucaparib	Vinorelbine
Capecitabine	Eribulin	Lanreotide	Osimertinib	Sonidegib	Vismodegib
Carboplatin	Erlotinib	Lapatinib		Sorafenib	
Carmustine		Letrozole		Streptozocin	

For information on ordering please contact: [844.232.4719](tel:844.232.4719), info@paradigmdx.com, or download and submit a requisition from our website at www.paradigmdx.com.

