Paradigm Cancer Diagnostic (PCDx)

Right options. Right now.

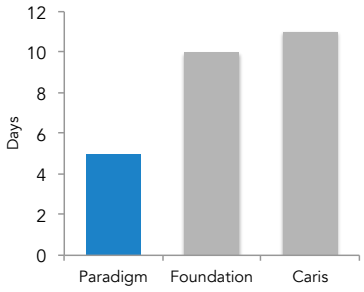
refuse to wait

Every day matters. PCDx is the fastest test available, providing results in 5 days. The PCDx test is designed for smaller batch sizes. This means your specimen is run right away rather than waiting for a large batch of samples to accumulate. Each step in our process is optimized for speed. For example, PCDx uses the Illumina NextSeq, which generates results in 25 hours compared to 3.5 days for a HighSeq.

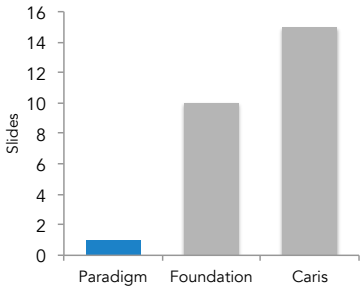
useful answers

We screen for an industry-leading >90 drugs and make your options clear in a simple report tailored to the clinic. Our test is validated on the actual FFPE diagnostic blocks from the tumors characterized by TCGA. If you are a researcher who wants to dig deeper into your patients' results, we provide unprecedented access to literature, data and registry funding.

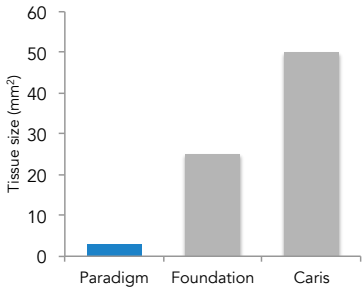
Testing time



NGS slides required



Minimum tissue size



Source: https://www.foundationmedicine.com/genomic-testing/foundation-one-cdx, https://www.carismolecularintelligence.com accessed 9/22/18

get results

We believe it is our job to get you results, not your responsibility to provide perfect specimens. PCDx is one of the most sensitive tests available, and we can make almost any specimen work including a single slide. We accomplish this with a proprietary library technique that converts five fold more DNA strands than other methods when 1.5 ng DNA is available. We use duplex UMI "barcodes" on each strand of DNA, a technique recently developed for low-yield cfDNA samples. Our proprietary informatics leverage the power of UMIs to detect variants with fewer DNA strands. When combined with more effective conversion of DNA, we need much less tissue.

About PCDx

PCDx is a comprehensive genomic profiling test designed to analyze solid tumor alterations to match the best therapies and clinical trials based on the latest clinical evidence in peer-reviewed literature.

Paradigm is able to accept most U.S. insurance plans, including Medicare. 43% of patients receiving therapy as directed by PCDx achieved a progression-free survival ratio of 1.3 compared to only 5% of patients treated by physician directed therapy[1].

[1]Oncotarget, 7(35), 56491-56500.

Indications

PCDx is indicated when a patient has:

a. a solid neoplasm; and
b. recurrent, relapsed, refractory, metastatic or advanced (stage III/IV) cancer; and
c. has not been tested by PCDx for the same cancer; and
d. has decided to seek further treatment

Rejection criteria

A specimen will be rejected when it:

a. contains less than 15% tumor cells after dissection; or
b. is smaller than a grain of rice (3mm^2) in size; or
c. has been decalcified (exception: EDTA); or
d. the specimen is not FFPE

Turnaround time	Sensitivity	Specificity	Drug associations
5 business days	≥99%	≥99%	>90 therapies

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Accuracy

Biomarker	Sensitivity	Specificity
SNVs, indels ≥7.5%	>99%	>99%
SNVs, indels ≥5.0%	>97%	>99%
Amplifications	>90%	>99%
IHC	>94%	>94%
MSI	>99%	>99%

Validation samples:
The original FFPE diagnostic specimens from tumors characterized by TCGA and FFPE cell line mixtures verified by a third party.

TMB cut-off is 10 mutations/MB

Associated Therapies

Abemaciclib
Abiraterone
Ado-trastuzumab emtansine
Afatinib
Alectinib
Anastrozole
Atezolizumab
Avelumab
Bevacizumab
Bicalutamide
Binimetinib
Brigatinib
Cabozantinib
Capecitabine
Carboplatin
Carmustine
Ceritinib
Cetuximab
Cisplatin
Crizotinib
Dabrafenib
Dacarbazine
Dacomitinib
Dasatinib
Diethylstilbestrol
Dinutuximab
Docetaxel
Doxorubicin
Durvalumab
Encorafenib
Enzalutamide
Epirubicin
Eribulin
Erlotinib
Everolimus
Exemestane
Fluorouracil
Flutamide
Fulvestrant
Gefitinib
Gemcitabine
Idelalisib
Imatinib
Interleukin-2
Ipilimumab
Irinotecan
Ketoconazole
Lapatinib
Lenvatinib
Letrozole
Liposomal Doxorubicin
Lorlatinib
Medroxy-progesterone
Megestrol
Mitomycin
Neratinib
Nilotinib
Nintedanib
Niraparib
Nivolumab
Olaparib
Olaratumab
Osimertinib
Oxaliplatin
Paclitaxel
Palbociclib
Panitumumab
Pazopanib
Pembrolizumab
Pemetrexed
Pertuzumab
Procarbazine
Regorafenib
Ribociclib
Rucaparib
Sonidegib
Sorafenib
Streptozocin
Sunitinib
Talazoparib
Tamoxifen
Temozolomide
Temsirolimus
Topotecan
Toremifene
Trametinib
Trastuzumab
Vandetanib
Vemurafenib
Vincristine
Vismodegib
Zoledronic acid

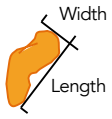
Specimen requirements

Preferred method

1. Verify tissue is as large as a grain of rice (3mm^2)

(actual size)

2. Send whole block



Alternate method

1. Measure tissue (length x width) in mm
area = _____ (Width) X _____ (Length) = _____ mm^2

2. If < 10mm^2, send whole block

3. If ≥ 10mm^2, send 4µm-5µm slides

Immunohistochemistry

Available

ALK
AR
CAIX
ER
hENT1
HER2/neu
IDO
MET
MGMT
MLH1
MSH2
MSH6
PD1
PD-L1
PMS2
PR
PTEN
RET
ROS1
TOPO1
TP
TRKpan
TS
TUBB3

Tumor-specific panels

Anal Carcinoma: PD-L1 (22C3), TP, TS, TUBB3, HER2, TRKpan
Appendix: TOP1, PD-L1 (22C3), MGMT, TRKpan, HER2, PTEN
Small Bowel: TOP1, PD-L1 (22C3), MGMT, TRKpan, HER2, PTEN
Bladder: PD-L1 (22C3), hENT1, TP, TUBB3, TS, TRKpan
Bone Cancer: PD-L1 (22C3), TOP1, MGMT, CAIX, HER2, TRKpan
Breast: AR, PD-L1, TP, TOP1, CAIX, TRKpan
CNS/brain cancers: MGMT, PD-L1 (22C3), CAIX, TOP1, TRKpan, ALK
Cervical: PD-L1 (22C3), CAIX, hENT1, TOP1, TS, TRKpan
Colorectal: PD-L1, HER2, MGMT, TRKpan, TOP1, PTEN
Gastric: HER2, PD-L1 (22C3), PTEN, TS, TUBB3, TRKpan
GIST: PD-L1 (22C3), TRKpan, HER2, MET, ALK, ROS1
Head and Neck: PD-L1 (22C3), MET, TUBB3, hENT1, PTEN , TRKpan
Hepatobiliary: hENT1, HER2, TP, PD-L1 (22C3), TOP1, TRKpan
Kidney: PD-L1 (22C3), MET, CAIX, hENT1, TUBB3, TRKpan

Tumor-specific panels

Mesothelioma: PD-L1 (22C3), hENT1, ALK, CAIX, TP, TRKpan
MMR: MLH1, MSH2, MSH6, PMS2
NSCLC: PD-L1, ALK, ROS1, hENT1, PTEN, TRKpan
Neuroendocrine: PD-L1 (22C3), MGMT, PTEN, TP, CAIX, TRKpan
Ovarian: PD-L1 (22C3), ER, HER2, TOP1, TUBB3, TRKpan
Pancreatic: hENT1, PD-L1 (22C3), MGMT, PTEN, TOP1, TRKpan
Prostate: AR, PTEN, PD-L1 (22C3), TUBB3, TRKpan, hENT1
Sarcoma: PD-L1 (22C3), TRKpan, CAIX, TUBB3, TOP1, MGMT
Skin (non-melanoma): PD-L1 (22C3), TP, TS, CAIX, hENT1, TRKpan
SCLC: PD-L1 (22C3), TOP1, HER2, MGMT, hENT1, TRKpan
Thyroid: PD-L1 (22C3), ALK, hENT1, TOP1, TUBB3, TRKpan
Uterine: ER, PD-L1 (22C3), PR, MGMT, TUBB3, TRKpan
Other: PD-L1 (22C3), HER2, hENT1, TOP1, TUBB3, TRKpan

234 gene NGS panel

ABCB1	APC	B2M	CCNE1	CSF1R	EPCAM	FANCA	FGFR3	HNF1A	KRAS	MRE11A	NOTCH3	PIK3R1	RBM10	SMAD4	TSC1
ABCC1	APLNR	BAP1	CD274	CTLA4	EPHA5	FANCC	FGFR4	HRAS	MAF	MSH2	NPM1	PLCB4	RECQL	SMARCA4	TSC2
ABCC2	AR	BARD1	CDA	CTNNB1	EPHA7	FANCD2	FLT3	HSD3B1	MAP2K1	MSH6	NRAS	PLCG1	RET	SMARCB1	TSHR
ABL1	ARAF	BCOR	CDC73	CYP19A1	ERBB2	FANCE	FLT4	IDH1	MAP2K2	MTHFR	NTRK1	PMS2	RHEB	SMO	TYMS
ADAMTS1	AREG	BNIP3	CDH1	CYP1A1	ERBB3	FANCF	FOXL2	IDH2	MAP3K1	MTOR	NTRK2	POLD1	RICTOR	SOCS1	VEGFA
ADAMTS16	ARID1A	BRAF	CDK12	CYP2D6	ERBB4	FANCG	FUBP1	IGF1R	MAPK1	MUTYH	NTRK3	POLE	RIT1	SPOP	VHL
ADAMTS18	ARID1B	BRCA1	CDK4	CYP3A4	ERCC1	FANCM	GATA3	IKZF1	MAPK3	MYC	PALB2	PPP2R1A	RNF43	STAG2	WT1
ADAMTS6	ARID2	BRCA2	CDK6	CYSLTR2	ERCC2	FAT1	GLI1	JAK1	MAPKAPK5	MYCN	PBRM1	PTCH1	ROS1	STAT3	XRCC1
ADAMTS9	ATM	BRIP1	CDKN2A	DCK	ERCC3	FBXW7	GNA11	JAK2	MDM2	MYOD1	PDCD1LG2	PTEN	RPTOR	STK11	YES1
ADAMTSL1	ATR	BTK	CHEK1	DDR2	ERRFI1	FCGR2A	GNAQ	JAK3	MDM4	NBN	PDGFRA	PTPN11	RRM1	SUFU	
AKT1	ATRX	BUB1B	CHEK2	DICER1	ESR1	FGD4	GNAS	KDM5C	MED12	NF1	PDGFRB	RAD50	SDHB	TERT-p	
AKT2	AURKA	CBL	CHFR	DNMT3A	ESR2	FGF3	GSTP1	KDM6A	MEN1	NF2	PIK3CA	RAD51C	SDHC	TGFBR2	
AKT3	AURKB	CCND1	CHKA	EGFR	EWSR1	FGF4	GSTT1	KDR	MET	NFE2L2	PIK3CB	RAD51D	SETD2	TNFAIP3	
ALK	AXIN1	CCND2	CIC	EMSY	EZH2	FGFR1	HDAC2	KEAP1	MGMT	NOTCH1	PIK3CD	RAF1	SF3B1	TOP2A	
AMER1	AXL	CCND3	CREBBP	EP300	FAM175A	FGFR2	HGF	KIT	MLH1	NOTCH2	PIK3CG	RB1	SMAD2	TP53	

Genetic structures tested: single nucleotide variants (SNVs) and insertions/deletions up to 40bp in coding regions of genes listed above. UTRs and splice junctions when actionable (e.g., MET exon 14 skipping). Mutation burden (SNVs, insertions, deletions) based on ~1 megabase.