Paradigm Cancer Diagnostic (PCDx)

Right options. Right now.

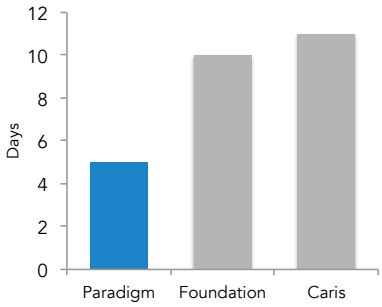
refuse to wait

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.

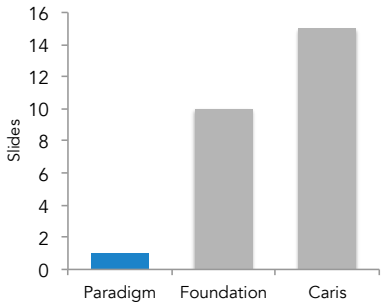
useful answers

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.

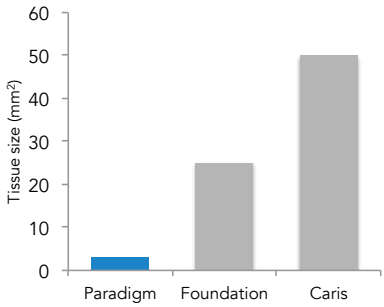
Testing time



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%
TMB	>85%	>92%

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

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, 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, Medroxyprogesterone, 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, Tamoxifen, Temozolomide, Temsirolimus, Topotecan, Toremifene, Trametinib, Trastuzumab, Vandetanib, Vemurafenib, Vincristine, Vismodegib, Zoledronic acid

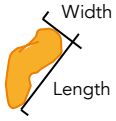
Specimen requirements

Preferred method

1. Verify tissue is as large as a grain of rice (3mm²)

(actual size)

2. Send whole block



Alternate method

1. Measure tissue (length x width) in mm
   area = _____ (Width) X _____ (Length) = _____ mm²
2. If < 25mm², send whole block
3. If ≥ 25mm², send 4µm-5µm slides

Immuno

TMB ~ 1Mb

PD-L1 TILs

PD-L1 tumor

MMR

Legacy mRNA panel

AR, AREG, ARID1A, BAD, BAX, BCL2, BIRC5, BRCA1, CA9, CDA, CDH1, CES2, CHUK, DCK, DHFR, DPYD, EPHA2, ERBB2, ERBB3, ERCC1, EREG, ESR1, EZH2, FGFR1, IGF1R, KDR, KIT, LRP6, MET, MGMT, MITF, MTOR, NFKB1, PARP1, PDGFRB, PGR, PTEN, PTGS2, PTPN6, RELA, RPS6KB1, RRM1, SLC29A1, SSTR2, TNFSF13, TOP2A, TUBB3, TYMP, TYMS, VEGFA

Immunohistochemistry

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

PCDx IHC Panels

Breast	AR, PD-L1, TP, TOPO1, MMR, TRKpan
Colorectal	MMR, PD-L1, TRKpan, HER2
NSCLC	PD-L1, ALK, ROS1, hENT1, TRKpan, MMR
Other	hENT1, HER2, MMR, PD-L1, TRKpan

MMR includes MLH1, MSH2, MSH6 and PMS2

234 gene NGS panel

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

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.