NeXT Dx®

REACH THE SUMMIT OF ADVANCED THERAPY SELECTION

We help you see what others miss.

WHOLE EXOME (DNA) + WHOLE TRANSCRIPTOME (RNA) + TUMOR-NORMAL

RNA-based fusion detection for certain cancers and patients is recommended by ASCO®[1] provisional clinical opinions and suggested by NCCN Guidelines®.[2]

Optimized RNA fusion detection

- **15%–30% more fusions detected than DNA[3,4]**
- **Deeper coverage with 200M total reads[5]**

Personalized Tumor-Normal approach

- **Eliminates false positives attributable to germline**
- **25%–30% fewer false positives than Tumor-Only testing[5]**

Gold standard TMB detection*

- **Exome-wide TMB provides greater accuracy than panel-based testing***
- **21%–44% of patients misclassified as TMB-high with Tumor-Only[6]**

High accuracy with >99% sensitivity[5] and >99% specificity[5]**

*according to Friends of Cancer Research[7,8] **aggregate sensitivity across all variant types

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Discover advanced therapy selection testing at www.personalis.com/products/next-dx/

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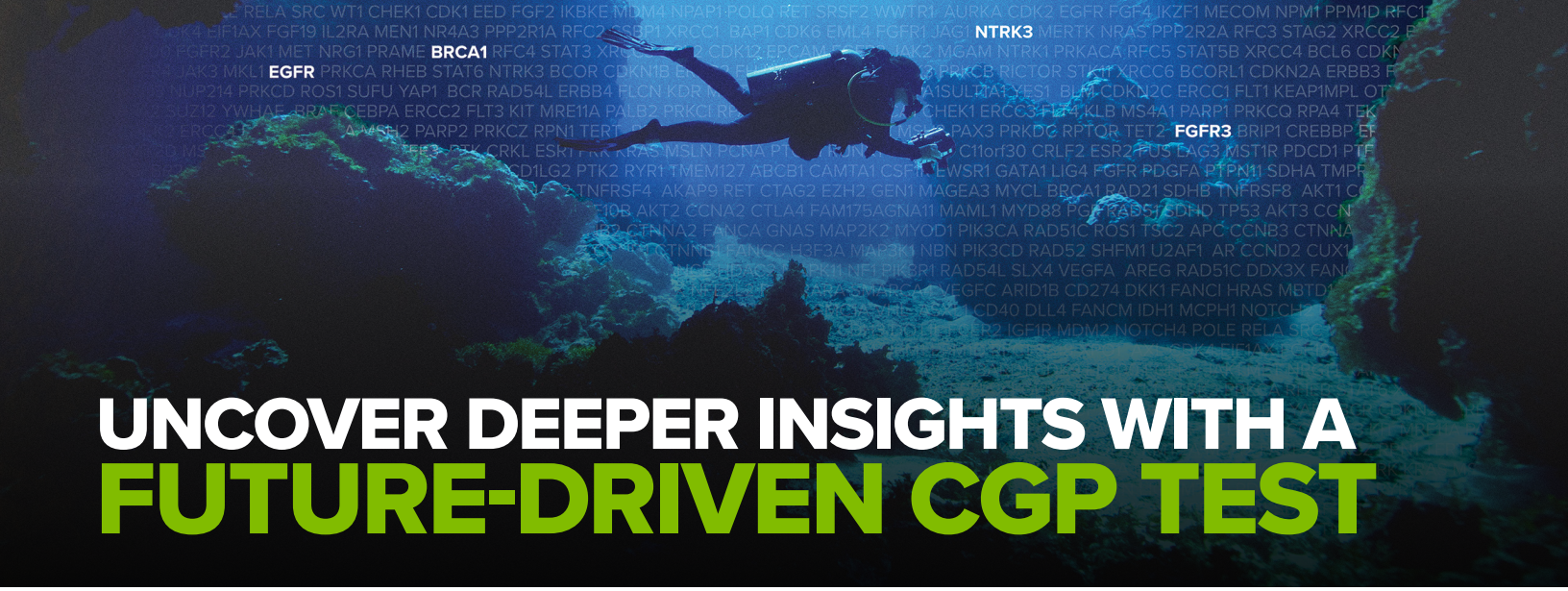
COLLEGE of AMERICAN PATHOLOGISTS

Personalis®



UNCOVER DEEPER INSIGHTS WITH A FUTURE-DRIVEN CGP TEST

Easy-to-interpret clinical report

Patient: John Doe
Report Released: 8/16/23 11:25:10
Accession Number: NYS1234
DOB: 01/01/01 **MRN:** 12345678

NeXT Dx®

Personalis NeXT Dx Report
Tumor + Matched Normal Analysis

Ordering Clinician	Specimen	Patient
Referring Physician: Personalis **Pathologist:** Rosalind Franklin **Institution:** New York State	**Accession #:** NYS1234 **Specimen ID:** SPEC-123 **Specimen Type:** FFPE **Collected:** 7/27/23 **Received:** 8/2/23 **Purity:** 75%[1] **Limiting Specimen Conditions:** None **Normal Specimen Type:** Blood **Collected:** 7/28/23 **Received:** 8/2/23	**Name:** John Doe **DOB:** 01/01/01 **Gender:** M **MRN:** 12345678 **Diagnosis:** Colon Adenocarcinoma **Primary Tumor Site:** Colon

I. GENOMIC ALTERATIONS SUMMARY

Detected Alterations with Clinical Relevance

Gene	Alteration	Drugs Associated with Sensitivity - Patient's Tumor Type	Drugs Associated with Resistance - Patient's Tumor Type	Drugs Associated with Sensitivity - Other Tumor Types	Clinical Trials	Allele Fraction[2]	Origin
BRCA2	N1784fs c.5351delA	None	None	olaparib, rucaparib, talazoparib, niraparib	**Yes**	35.6%	Germline
KRAS	G12D c.35G>A	None	panitumumab, cetuximab,	None	**Yes**	13.20%	Somatic
PIK3CA	E545K c.1633G>A	None	None	alpelisib + fulvestrant	**Yes**	7.70%	Somatic

***BRCA2 N1784fs: this gene is associated with homologous recombination repair (HRR)**

Germline Alterations[3]

Gene	Alteration	Clinical Significance	Notes
BRCA2	N1784fs c.5351delA	**Pathogenic**	Referral to a cancer genetics provider for genetic counseling and confirmatory testing is recommended.

Other Biomarkers Tested

Biomarker	Result	Drugs Associated with Sensitivity -Patient's Tumor Type	Drugs Associated with Resistance -Patient's Tumor Type	Drugs Associated with Sensitivity - Other Tumor Types	Clinical Trials
Microsatellite instability (MSI)	Positive, High (MSI-H)	dostarlimab, ipilimumab + nivolumab, nivolumab, pembrolizumab	None	avelumab	**Yes**
Tumor mutation burden (TMB)	19.36 muts/Mb	See section IV	None	See section IV	See section IV

Alterations of unknown clinical significance were detected; please refer to section V for details.

Clinically Relevant Biomarkers Not Detected
BRAF, ERBB2, NRAS, NTRK1, RET

[1] Specimen purity (tumor content) is determined through histopathology by a licensed molecular pathologist (refer to Appendix B).
[2] Allele Fraction refers to the fraction of the total sample wherein the variant allele was detected. This value is not adjusted for specimen purity.
[3] Germline alterations are reported from select genes as incidental findings. Please see section VI Report Details for the list of genes.

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Actionable variants, approved therapies

Clinical trial options, variant origin

Incidental germline findings

MSI and TMB

Relevant negatives by tumor type

Test performance specifications

Sensitivity	
Single nucleotide variants (at mutant allele frequency ≥5%)	>99%
Small insertions and deletions (at mutant allele frequency ≥5%)	>98%
Copy number alterations (at ≥30% tumor content)	98%
Gene fusions	96%
Positive predictive value*	
Single nucleotide variants (at mutant allele frequency ≥5%)	>99%
Small insertions and deletions (at mutant allele frequency ≥5%)	>99%
Copy number alterations (at ≥30% tumor content)	>99%
Gene fusions	>98%
Additional assay specifications	
Microsatellite instability (MSI)**	>99% accuracy
Tumor mutation burden (TMB)†	Calculated from whole exome by measuring the number of mutations per megabase (mut/Mb) is reported
Splice variants reporting from RNA	MET exon 14 skipping mutations
HLA typing	HLA typing results are reported using normal sample
Type of sequencing	DNA and RNA sequencing using whole exome and transcriptome sequencing
Typical median depth Whole exome (tumor) Boosted region (247 cancer-related genes) (tumor) Whole exome (blood or saliva as matched normal samples) Whole transcriptome (tumor)	 ~500X >1500X ~150X 200M total reads
Sample types††	Tumor: FFPE Normal: blood or saliva
Regions analyzed	Coding and relevant non-coding regions of 401 genes
Turn around time	About 2 weeks from sample receipt
Test requisition form required	Yes

* Positive predictive value is calculated by comparing variants detected by the NeXT Dx® Test to those detected by a validated TSO500 test.
** MSI status is determined by measuring nucleotide repeats from 117 loci.
† TMB is reported as the number of mutations per megabase (muts/Mb) from tumor-normal analysis. Please note that there is currently no standard cut-off to define a high TMB for different tumor types.
†† Decalcified bone is not an acceptable specimen. Additionally, specimens collected in New York State are not acceptable at this time.

NeXT Dx® reportable gene list

Single nucleotide variants, small insertions and deletions, copy number alterations, and gene fusions involving the genes below may be reported in the test.

ABCB1†	*CAMTA1*†	*CSF1R*†	*EWSR1*†	*GATA1*†	*LIG4*	*MUTYH*†	*PDGFA*	*PTPN11*†	*SDHA**	*TMPRSS2*†
ABL1†	*CBFB*†	*CSF3R*†	*EXO1*	*GATA2**†	*LRP1B*	*MYC*†	*PDGFB*†	*PVRL4*†	*SDHAF2**	*TNFRSF4*†
AKAP9†	*CBL*†	*CTAG2*†	*EZH2*†	*GEN1*	*MAGEA3*†	*MYCL*	*PDGFRA***	*RAD21*†	*SDHB***	*TNFRSF8*†
AKT1†	*CCNA1*	*CTDNEP1*	*EZHIP*†	*GLI2*†	*MAGEA4*†	*MYCN*†	*PDGFRB*†	*RAD50***	*SDHC***	*TNFRSF10B*
AKT2†	*CCNA2*	*CTLA4*†	*FAM175A*	*GNA11*†	*MAML1*	*MYD88*†	*PGR*†	*RAD51*†	*SDHD***	*TP53***
AKT3†	*CCNB1*	*CTNNA1*	*FAN1*	*GNAQ*†	*MAP2K1*†	*MYH11*†	*PHF1*†	*RAD51B*†	*SETBP1*†	*TSC1***
*ALK***	*CCNB2*	*CTNNA2*	*FANCA*†	*GNAS*†	*MAP2K2*†	*MYOD1*†	*PIK3CA***	*RAD51C***	*SETD2*	*TSC2***
*APC***	*CCNB3*†	*CTNNA3*	*FANCB*†	*GPNMB*†	*MAP2K4*†	*NAB2*†	*PIK3CB*†	*RAD51D***	*SF3B1*†	*TYRO3*
APOBEC3B	*CCND1*†	*CTNNB1*†	*FANCC*†	*H3F3A*	*MAP3K1*†	*NBN*	*PIK3CD*†	*RAD52*	*SHFM1*	*U2AF1*†
AR†	*CCND2*†	*CUX1*†	*FANCD2*†	*HDAC1*	*MAPK1*†	*NCSTN*	*PIK3CG*†	*RAD54B*	*SHH*†	*USH2A*
ARAF†	*CCND3*†	*DDR2*†	*FANCE*†	*HDAC2*	*MAPK11*	*NF1***	*PIK3R1*†	*RAD54L*	*SLX4*†	*VEGFA*†
AREG†	*CCNE1*†	*DDX3X*	*FANCF*†	*HEY1*†	*MAPK3*	*NF2***	*PIK3R2*	*RAF1*†	*SMAD4***	*VEGFB*†
ARID1A†	*CCNE2*	*DEK*†	*FANCG*†	*HNF1A*†	*MAX**	*NFE2L2*†	*PML*†	*RARA*†	*SMARCA4*†	*VEGFC*
ARID1B	*CD274*†	*DKK1*†	*FANCI*†	*HRAS*†	*MBTD1*†	*NKX2-1*†	*PMS1*	*RB1***	*SMARCB1*†	*VGLL2*†
ARID2	*CD276*†	*DLL3*†	*FANCL*†	*HSP90AA1*†	*MCL1*†	*NOTCH1*†	*PMS2***	*RBBP8*	*SMC1A*†	*VHL***
ASXL1†	*CD40*†	*DLL4*	*FANCM*†	*IDH1*†	*MCPH1*	*NOTCH2*†	*POLD1**	*RBM15*†	*SMC3*†	*WEE1*†
*ATM***	*CDH1***	*DNMT3A*†	*FBXW7*†	*IDH2*†	*MDC1*	*NOTCH3*†	*POLD2*	*RECQL4*	*SMO*†	*WRN*
ATR†	*CDH3*†	*DOT1L*	*FCER2*†	*IGF1R*†	*MDM2*†	*NOTCH4*	*POLE***	*RELA*†	*SRC*†	*WT1***
ATRX†	*CDK1*	*EED*	*FGF2*†	*IKBKE*	*MDM4*†	*NPAP1*	*POLQ*	*RET***	*SRSF2*†	*WWTR1*†
AURKA†	*CDK2*	*EGFR***	*FGF4*	*IKZF1*†	*MECOM*†	*NPM1*†	*PPM1D*	*RFC1*	*SS18*†	*XPO1*†
AXL†	*CDK4***	*EIF1AX*	*FGF19*†	*IL2RA*†	*MEN1***	*NR4A3*†	*PPP2R1A*	*RFC2*	*SSBP1*	*XRCC1*†
*BAP1***	*CDK6*†	*EML4*†	*FGFR1*†	*JAG1*	*MERTK*	*NRAS*†	*PPP2R2A*	*RFC3*	*STAG2*†	*XRCC2*
*BARD1**	*CDK9*†	*EP300*†	*FGFR2*†	*JAK1*†	*MET***	*NRG1*†	*PRAME*†	*RFC4*	*STAT3*†	*XRCC3*
BCL2†	*CDK12*	*EPCAM*†	*FGFR3*†	*JAK2*†	*MGAM*	*NTRK1*†	*PRKACA*†	*RFC5*	*STAT5B*†	*XRCC4*
BCL6†	*CDKN1A*†	*EPHA2*	*FGFR4*†	*JAK3*†	*MKL1*†	*NTRK2*†	*PRKCA*†	*RHEB*	*STAT6*†	*XRCC5*
BCOR†	*CDKN1B***	*ERBB2*†	*FH***	*KDM5C*	*MLH1***	*NTRK3*†	*PRKCB*†	*RICTOR*†	*STK11***	*XRCC6*
BCORL1†	*CDKN2A***	*ERBB3*†	*FIGF*	*KDM6A*†	*MLH3*	*NUP214*†	*PRKCD*†	*ROS1*†	*SUFU**	*YAP1*†
BCR†	*CDKN2B*†	*ERBB4*†	*FLCN***	*KDR*†	*MLLT3*†	*NUTM2A*†	*PRKCE*†	*RPA1*	*SULT1A1*†	*YES1*†
BLM	*CDKN2C*	*ERCC1*	*FLT1*†	*KEAP1*	*MPL*†	*OTX2*	*PRKCG*†	*RPA2*	*SUZ12*†	*YWHAE*†
BRAF†	*CEBPA***	*ERCC2*	*FLT3*†	*KIT***	*MRE11A***	*PALB2***	*PRKCI*†	*RPA3*	*SYK*†	*ZMYM3*
*BRCA1***	*CHEK1*†	*ERCC3*	*FLT4*†	*KLB*†	*MS4A1*†	*PARP1*†	*PRKCQ*†	*RPA4*	*TEK*	*ZRSR2*†
*BRCA2***	*CHEK2***	*ERCC4*	*FOLR1*†	*KMT2A*†	*MSH2***	*PARP2*	*PRKCZ*†	*RPN1*†	*TERT***	
BRD4†	*CIC*†	*ERCC5*	*FOXL2*†	*KMT2C*	*MSH3*	*PAX3*†	*PRKDC*	*RPTOR*	*TET2*†	
*BRIP1***	*CREBBP*†	*ERCC6*	*FOXO1*†	*KMT2D*	*MSH6***	*PBRM1*	*PSCA*†	*RTEL1**	*TFE3*†	
BTK†	*CRKL*†	*ESR1*†	*FRK*	*KRAS*†	*MSLN*†	*PCNA*	*PTCH1***	*RUNX1***	*TGFBR1*†	
C11orf30	*CRLF2*†	*ESR2*†	*FUS*†	*LAG3*†	*MST1R*	*PDCD1*†	*PTEN***	*RUNX1T1*†	*TGFBR2*†	
CALR†	*CRTC1*†	*ETV6***	*FYN*†	*LIG3*	*MTOR*†	*PDCD1LG2*†	*PTK2*†	*RYR1*	*TMEM127**	

* Represents genes in which likely pathogenic/pathogenic germline variants will be reported, in addition to somatic variants, as incidental findings
† Represents fusion genes

Regulatory Compliance Information: The NeXT Dx® test is a next-generation sequencing (NGS) based laboratory developed test (LDT) for cancer patients with solid tumors. The NeXT Dx® test is performed in the CLIA/CAP accredited Personalis® Clinical Laboratory. The NeXT Dx® test was developed and performance characteristics determined by the Personalis® Clinical Laboratory, which is qualified to perform high-complexity clinical testing. The NeXT Dx® test has not been cleared or approved by the FDA. The NeXT Dx® test reports on 401 genes.

1 Chakravarty D et al. *J Clin Oncol.* 2022 Apr 10;40(11):1231-1258. **2** Updated NCCN guidelines® for NSCLC (Source: nccn.org/professionals/physician_gls/pdf/nscl.pdf) **3** Michuda J et al. *Journal of Clinical Oncology* 40, no. 16_suppl (June 01, 2022) 3077. **4** Benayed R et al. *Clin Cancer Res* 2019, 25(15) 4712-22. **5** Internal data on file. **6** Nassar AH et al. *Cancer Cell.* 2022;40(10):1161-1172.e5. **7** Merino DM et al. *J Immunother Cancer*. 2020;8(1):e000147. **8** Vega DM et al. *Ann Oncol*. 2021;32(12):1626-1636.

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