xT Validation

The Tempus xT next generation sequencing assay is designed to detect actionable oncologic targets by sequencing tumor samples with matched normal saliva or blood samples, when available.

The xT assay[1] covers 648 genes spanning ~3.6 Mb of genomic space. From tissue sequencing, xT detects somatic single nucleotide variants (SNVs) and insertions and deletions (indels), and may also report potential germline SNVs and indels from the buffy coat normal match process. Additionally, xT detects copy number variants (CNVs) and translocations in 22 genes are detected, along with the TERT promoter region and 239 sites to determine microsatellite instability status. Tumor mutational burden (TMB) and microsatellite instability (MSI) status are reported. HLA Class I genotyping information is provided on xT tumor normal and tumor only reports for clinical trial matching purposes only, and not for transplantation purposes. Test results are intended to provide tumor molecular information that can be used by clinicians to help inform clinical management when patients are seeking further cancer treatment.

CAP/CLIA validation of the Tempus xT panel in its Chicago, Illinois and Durham, North Carolina laboratories focused on actionable oncologic variants. The assay requires specimens with a tumor content of 20% post macrodissection (minimum 30% for MSI status). For solid tumors, an FFPE tumor sample is sequenced along with a matched normal blood or saliva sample (when available). For circulating hematologic malignancies, a blood or bone marrow sample is sequenced. Clinical sequencing is performed to 500x depth of coverage for tumor specimens and 150x for normal specimens. Performance specifications are listed in Tables 1 and 2 below. These results establish high sensitivity and negative percentage agreement for the Tempus xT assay. The orthogonal reference methods used for xT.v4 were previous versions of the Tempus xT assay. The xT assay is used across a diverse set of clinical settings including leading academic centers, NCI designated cancer centers, hospital networks, and community hospitals.

xT PERFORMANCE SPECIFICATIONS—CHICAGO LAB*

Variant Class	Limit of Detection	Analytical Sensitivity	Negative Percentage Agreement
SNVs	5.0% VAF	98.2%	>99.0%
Indels	5.0% VAF	91.1%	>99.0%
Copy Number Alterations	Gain: 30.0% Tumor Purity Loss: 40.0% Tumor Purity	91.4%	>99.0%
Microsatellite Instability	30.0% Tumor Purity	90.5%	98.4%
Rearrangements	30.0% Tumor Purity	90.9%	>99.0%

xT PERFORMANCE SPECIFICATIONS—DURHAM LAB*

Variant Class	Limit of Detection	Analytical Sensitivity	Negative Percentage Agreement
SNVs	5.0% VAF	97.6%	>99.0%
Indels	5.0% VAF	91.4%	>99.0%
Copy Number Alterations	Gain: 33.2% Tumor Purity Loss: 38.5% Tumor Purity	92.7%	>99.0%
Microsatellite Instability	30.0% Tumor Purity	96.2%	99.6%
Rearrangements	30.0% Tumor Purity	96.3%	>99.0%

*Solid tumor performance

xT Gene List

ABCB1	*BCR*	*CHD2*	*(TCEB1)*	*FCGR3A*	*GRIN2A*	*IFNAR1*	*MAD2L2*	*NFKBIA*	*PIK3R1*	*RHOA*	*SPOP*	*TSHR*
ABCC3	*BIRC3*	*CHD4*	*EMSY*	*FDPS*	*GRM3*	*IFNAR2*	*MAF*	*NHP2*	*PIK3R2* ‡	*RICTOR*	*SPRED1*	*TUSC3*
ABL1	*BLM*	*CHD7*	*ENG*	*FGF1*	*GSTP1*	*IFNGR1*	*MAFB*	*NKX2-1*	*PIM1*	*RINT1*	*SRC*	*TYMS*
ABL2	*BMPR1A* ***	*CHEK1*	*EP300*	*FGF10*	*H19*	*IFNGR2*	*MAGI2*	*NOP10*	*PLCG1*	*RIT1*	*SRSF2*	*U2AF1*
ABRAXAS1	*BRAF*	*CHEK2* ***	*EPCAM* ***,‡	*FGF14*	*H3F3A*	*IFNL3*	*MALT1*	*NOTCH1*	*PLCG2*	*RNF139*	*STAG2*	*UBE2T*
ACTA2	*BRCA1* ***	*CIC*	*EPHA2*	*FGF2*	*HAS3*	*IKBKE*	*MAP2K1*	*NOTCH2*	*PML*	*RNF43*	*STAT3*	*UGT1A1*
ACVR1 (ALK2)	*BRCA2* ***	*CIITA*	*EPHA7*	*FGF23*	*HAVCR2*	*IKZF1*	*MAP2K2*	*NOTCH3*	*PMS1*	*ROS1*	*STAT4*	*UGT1A9*
ACVR1B	*BRD4*	*CKS1B*	*EPHB1*	*FGF3*	*HDAC1*	*IL10RA*	*MAP2K4*	*NOTCH4*	*PMS2* ***	*RPL5*	*STAT5A*	*UMPS*
AGO1	*BRIP1* ***	*CREBBP*	*EPHB2*	*FGF4*	*HDAC2*	*IL15*	*MAP3K1*	*NPM1*	*POLD1* ***	*RPS15*	*STAT5B*	*VEGFA*
AJUBA	*BTG1*	*CRKL*	*EPOR*	*FGF5*	*HDAC4*	*IL2RA*	*MAP3K7*	*NQO1*	*POLE* ***	*RPS6KB1*	*STAT6*	*VEGFB*
AKT1	*BTK*	*CRLF2*	*ERBB2 (HER2)*	*FGF6*	*HGF*	*IL6R*	*MAPK1*	*NRAS*	*POLH*	*RPTOR*	*STK11* ***	*VHL* ***
AKT2	*BUB1B*	*CSF1R*	*ERBB3*	*FGF7*	*HIF1A*	*IL7R*	*MAX* ***	*NRG1*	*POLQ*	*RRM1*	*SUFU* ***	*VSIR*
AKT3	*C11orf65*	*CSF3R*	*ERBB4*	*FGF8*	*HIST1H1E*	*ING1*	*MC1R*	*NSD1*	*POT1*	*RSF1*	*SUZ12*	*WEE1*
ALK	*C3orf70*	*CTC1*	*ERCC1*	*FGF9*	*HIST1H3B*	*INPP4B*	*MCL1*	*NSD2*	*POU2F2*	*RUNX1* ***	*SYK*	*WNK1*
AMER1	*C8orf34*	*CTCF*	*ERCC2*	*FGFR1*	*HIST1H4E*	*IRF1*	*MDM2*	*NT5C2*	*PPARA*	*RUNX1T1*	*SYNE1*	*WNK2*
APC ***	*CALR*	*CTLA4*	*ERCC3*	*FGFR2*	*HLA-A*	*IRF2*	*MDM4*	*NTHL1* ***	*PPARD*	*RXRA*	*TAF1*	*WRN*
APLNR	*CARD11*	*CTNNA1*	*ERCC4*	*FGFR3*	*HLA-B*	*IRF4*	*MED12*	*NTRK1*	*PPARG*	*SCG5*	*TANC1*	*WT1* ***
APOB	*CARM1*	*CTNNB1*	*ERCC5*	*FGFR4*	*HLA-C*	*IRS2*	*MEF2B*	*NTRK2*	*PPM1D*	*SDHA* ***	*TAP1*	*XPA*
AR	*CASP8*	*CTRC*	*ERCC6*	*FH* ***	*HLA-DMA*	*ITPKB*	*MEN1* ***	*NTRK3*	*PPP1R15A*	*SDHAF2* ***	*TAP2*	*XPC*
ARAF	*CASR*	*CUL1*	*ERG*	*FHIT*	*HLA-DMB*	*JAK1*	*MET* ***	*NUDT15*	*PPP2R1A*	*SDHB* ***	*TARBP2*	*XPO1*
ARHGAP26	*CBFB*	*CUL3*	*ERRFI1*	*FLCN* ***	*HLA-DOA*	*JAK2*	*MGMT*	*NUP98*	*PPP2R2A*	*SDHC* ***	*TBC1D12*	*XRCC1*
ARHGAP35	*CBL*	*CUL4A*	*ESR1*	*FLT1*	*HLA-DOB*	*JAK3*	*MIB1*	*OLIG2*	*PPP6C*	*SDHD* ***	*TBL1XR1*	*XRCC2*
ARID1A	*CBLB*	*CUL4B*	*ETS1*	*FLT3*	*HLA-DPA1*	*JUN*	*MITF*	*P2RY8*	*PRCC*	*SEC23B*	*TBX3*	*XRCC3*
ARID1B	*CBLC*	*CUX1*	*ETS2*	*FLT4*	*HLA-DPB1*	*KAT6A*	*MKI67*	*PAK1*	*PRDM1*	*SEMA3C*	*TCF3*	*YEATS4*
ARID2	*CBR3*	*CXCR4*	*ETV1*	*FNTB*	*HLA-DPB2*	*KDM5A*	*MLH1* ***	*PALB2* ***	*PREX2*	*SETBP1*	*TCF7L2*	*ZFHX3*
ARID5B	*CCDC6*	*CYLD*	*ETV4*	*FOXA1*	*HLA-DQA1*	*KDM5C*	*MLH3*	*PALLD*	*PRKAR1A* ***	*SETD2*	*TCL1A*	*ZMYM3*
ASNS	*CCND1*	*CYP1B1*	*ETV5*	*FOXL2*	*HLA-DQA2*	*KDM5D*	*MLLT3*	*NUP98*	*PRKDC*	*SF3B1*	*TERT* **	*ZNF217*
ASPSCR1	*CCND2*	*CYP2D6*	*ETV6* ***	*FOXO1*	*HLA-DQB1*	*KDM6A*	*MN1*	*OLIG2*	*PRKDC*	*SGK1*	*TET2*	*ZNF471*
ASXL1	*CCND3*	*CYP3A5*	*ETS1*	*FOXO3*	*HLA-DQB2*	*KDR*	*MPL*	*P2RY8*	*PRKN*	*SH2B3*	*TFE3* ‡	*ZNF620*
ATIC	*CCNE1*	*CYSLTR2*	*ETS2*	*FOXP1*	*HLA-DRA*	*KEAP1*	*MRE11*	*PAK1*	*PRSS1*	*SHH*	*TFEB*	*ZNF750*
ATM ***	*CD19*	*DAXX*	*ETV1*	*FOXQ1*	*HLA-DRB1*	*KEL*	*MS4A1*	*PAX3*	*PTCH1* ***	*SLC26A3*	*TFEC*	*ZNRF3*
ATP7B	*CD22*	*DDB2*	*ETV4*	*FRS2*	*HLA-DRB5*	*KIF1B*	*MSH2* ***	*PAX5*	*PTCH2*	*SLC47A2*	*TGFBR1*	*ZRSR2*
ATR	*CD274 (PD L1)*	*DDR2*	*ETV5*	*FUBP1*	*HLA-DRB6*	*KIT* ***	*MSH3* ***	*PAX7*	*PTEN* ***	*SLC9A3R1*	*TGFBR2*	
ATRX	*CD40*	*DDX3X*	*ETV6* ***	*FUS*	*HLA-E*	*KLF4*	*MSH6* ***	*PAX8*	*PTPN11*	*SLIT2*	*TIGIT*	
AURKA	*CD70*	*DICER1* ***	*EWSR1*	*G6PD*	*HLA-F*	*KLHL6*	*MTAP*	*PBRM1*	*PTPN13*	*SLX4*	*TMEM127* ***	
AURKB	*CD79A*	*DIRC2*	*EZH2*	*GABRA6*	*HLA-G*	*KLLN*	*MTHFD2*	*PCBP1*	*PTPN22*	*SMAD2*	*TMEM173*	
AXIN1	*CD79B*	*DIS3*	*FAM46C*	*GALNT12*	*HNF1A*	*KMT2A*	*MTHFR*	*PDCD1* ‡	*PTPRD*	*SMAD3*	*TMPRSS2*	
AXIN2 ***	*CDC73*	*DIS3L2*	*FANCA*	*GATA1*	*HNF1B*	*KMT2B*	*MTOR*	*PDCD1LG2*	*PTPRT*	*SMAD4* ***	*TNF*	
AXL	*CDH1* ***	*DKC1*	*FANCB*	*GATA2* ***	*HOXA11*	*KMT2C*	*MTRR*	*PDGFRA* ***	*RAD51*	*SMARCA1* ‡	*TNFAIP3*	
B2M	*CDK12*	*DNM2*	*FANCC*	*GATA3*	*HOXB13*	*KMT2D*	*MUTYH* ***	*PDGFRB*	*RAD51B*	*SMARCA4* ***	*TNFRSF14*	
BAP1 ***	*CDK4* ***	*DNMT3A*	*FANCD2*	*GATA4*	*HRAS*	*KRAS*	*MYB*	*PDK1*	*RAD51C* ***	*SMARCB1* ***	*TNFRSF17*	
BARD1 ***	*CDK6*	*DOT1L*	*FANCE*	*GATA6*	*HSD11B2*	*L2HGDH*	*MYC*	*PHF6*	*RAD51D* ***	*SMARCE1*	*TNFRSF9*	
BCL10	*CDK8*	*DPYD*	*FANCF*	*GEN1*	*HSD3B1*	*LAG3*	*MYCL*	*PHGDH*	*RAD54L*	*SMC1A*	*TOP1*	
BCL11B	*CDKN1A*	*DYNC2H1*	*FANCG*	*GLI1*	*HSD3B2*	*LATS1*	*MYCN*	*PHLPP1*	*RAF1*	*SMC3*	*TOP2A*	
BCL2	*CDKN1B*	*EBF1*	*FANCI*	*GLI2*	*HSP90AA1*	*LCK*	*MYD88*	*PHLPP2*	*RANBP2*	*SMO*	*TP53* ***	
BCL2L1	*CDKN1C*	*ECT2L*	*FANCL*	*GNA11*	*HSPH1*	*LDLR*	*MYH11*	*PHOX2B* ***	*RARA*	*SOCS1*	*TP63*	
BCL2L11	*CDKN2A* ***	*EGF*	*FANCM*	*GNA13*	*IDH1*	*LEF1*	*NBN*	*PIAS4*	*RASA1*	*SOD2*	*TPM1*	
BCL6	*CDKN2B*	*EGFR* ***	*FAS*	*GNAQ*	*IDH2*	*LMNA*	*NCOR1*	*PIK3C2B*	*RB1* ***	*SOX10*	*TPMT*	
BCL7A	*CDKN2C*	*EGLN1*	*FAT1*	*GNAS*	*IDO1*	*LMO1*	*NCOR2*	*PIK3CA*	*RBM10* ‡	*SOX2*	*TRAF3*	
BCLAF1 ‡	*CEBPA* ***	*EIF1AX*	*FBXO11*	*GPC3*	*IFIT1*	*LRP1B*	*NF1* ***	*PIK3CB*	*RECQL4*	*SOX9*	*TRAF7*	
BCOR	*CEP57*	*ELF3*	*FBXW7*	*GPS2*	*IFIT2*	*LYN*	*NF2* ***	*PIK3CD*	*RET* ***	*SPEN*	*TSC1* ***	
BCORL1	*CFTR*	*ELOC*	*FCGR2A*	*GREM1*	*IFIT3*	*LZTR1*	*NFE2L2*	*PIK3CG*	*RHEB*	*SPINK1*	*TSC2* ***	

GENE REARRANGEMENTS BY DNA SEQUENCING†

ABL1, ALK, BCR, BRAF, EGFR, ETV6, EWSR1, FGFR2, FGFR3, MYB, NRG1, NTRK1, NTRK2, NTRK3, PAX8, PDGFRA, PML, RARA, RET, ROS1, TFE3, TMPRSS2

1 NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic V.3.2024. © National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed [February 12, 2024]. To view the most recent and complete version of the guideline, go online to NCCN.org.

2 NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Genetic/Familial High-Risk Assessment: Colorectal V.2.2023. © National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed [October 30, 2023]. To view the most recent and complete version of the guideline, go online to NCCN.org.

** Includes promoter region

*** Genes in which potential germline findings are reported

In addition to reporting on somatic variants, when a normal sample is provided, Tempus reports germline potential findings on a limited set of variants associated with inherited cancer syndromes within 63 genes selected based on recommendations from the American College of Medical Genetics (ACMG), the National Comprehensive Cancer Network (NCCN), and/or published literature.

† Exons and select intronic regions only. Additional coverage information provided upon request.

‡ Genes that do not have full exon coverage of a primary transcript

Potential germline findings gene list

This list is composed of 63 genes associated with inherited cancer syndromes included on the xT panel and selected based on recommendations from the American College of Medical Genetics (ACMG), the National Comprehensive Cancer Network (NCCN) and/or published literature.[1,2] The primary focus of the xT panel is somatic reporting. Tempus also offers separately ordered validated germline hereditary cancer panels through two reference labs, Ambry Genetics® and GeneDx, for xG testing, with the choice of reference lab depending on various factors. As each test differs, please contact your Tempus representative for more details on the variances between GeneDx and Ambry testing, and which test your account may utilize.

APC: *APC-associated conditions*
ATM: *Ataxia-Telangiectasia, Breast cancer susceptibility, Pancreatic cancer susceptibility*
AXIN2: *Oligodontia-colorectal cancer syndrome*
BAP1: *BAP1 tumor predisposition syndrome*
BARD1: *Breast cancer susceptibility*
BMPR1A: *Juvenile polyposis syndrome*
BRCA1: *Hereditary breast and ovarian cancer syndrome, Fanconi anemia*
BRCA2: *Hereditary breast and ovarian cancer syndrome, Fanconi anemia*
BRIP1: *Ovarian cancer susceptibility, Fanconi anemia*
CDH1: *Hereditary diffuse gastric cancer syndrome*
CDK4: *Melanoma susceptibility*
CDKN2A: *Familial atypical multiple mole-melanoma syndrome*
CEBPA: *Acute myeloid leukemia susceptibility*
CHEK2: *Breast cancer susceptibility, Colon cancer susceptibility*
DICER1: *DICER1 tumor predisposition syndrome*
EGFR: *Lung cancer susceptibility, TKI resistance*
EPCAM [§]***:*** *Lynch syndrome*
ETV6: *MDS susceptibility, Leukemia susceptibility, thrombocytopenia susceptibility*
FH: *Hereditary leiomyomatosis and renal cell cancer syndrome, Fumarate hydratase deficiency*
FLCN: *Birt-Hogg-Dube syndrome*
GATA2: *GATA2 deficiency with susceptibility to myeloid malignancies*
KIT: *Gastrointestinal stromal tumor susceptibility*
MAX: *Hereditary paraganglioma-pheochromocytoma syndrome*
MEN1: *Multiple endocrine neoplasia type 1, Familial isolated hyperparathyroidism*
MET: *Hereditary papillary renal cell carcinoma*
MLH1: *Lynch syndrome, Constitutional mismatch repair deficiency*
MSH2: *Lynch syndrome, Constitutional mismatch repair deficiency*
MSH3: *MSH3-associated polyposis*
MSH6: *Lynch syndrome, Constitutional mismatch repair deficiency*
MUTYH: *MUTYH-associated polyposis*
NF1: *Neurofibromatosis type 1*
NF2: *NF2-related schwannomatosis*
NTHL1: *NTHL1 tumor syndrome*
PALB2: *Breast cancer susceptibility, Pancreatic cancer susceptibility, Ovarian cancer susceptibility, Fanconi anemia*
PDGFRA: *GIST-plus syndrome*
PHOX2B: *Congenital central hypoventilation syndrome, Neuroblastoma susceptibility*
PMS2: *Lynch syndrome, Constitutional mismatch repair deficiency*
POLD1 [§]***:*** *Polymerase proofreading-associated polyposis*
POLE [§]***:*** *Polymerase proofreading-associated polyposis*
PRKAR1A: *Carney complex*
PTCH1: *Gorlin syndrome, Basal cell nevus syndrome*
PTEN: *PTEN hamartoma tumor syndrome*
RAD51C: *Ovarian cancer susceptibility, Breast cancer susceptibility, Fanconi anemia*
RAD51D: *Ovarian cancer susceptibility, Breast cancer susceptibility*
RB1: *Retinoblastoma susceptibility*
RET: *Multiple endocrine neoplasia type 2, Familial medullary thyroid cancer*
RUNX1: *RUNX1 familial platelet disorder, Myeloid malignancy susceptibility*
SDHA: *Hereditary paraganglioma-pheochromocytoma syndrome, Leigh syndrome*
SDHAF2: *Hereditary paraganglioma-pheochromocytoma syndrome*
SDHB: *Hereditary paraganglioma-pheochromocytoma syndrome, Mitochondrial complex II deficiency*
SDHC: *Hereditary paraganglioma-pheochromocytoma syndrome*
SDHD: *Hereditary paraganglioma-pheochromocytoma syndrome*
SMAD4: *Juvenile polyposis, Hereditary hemorrhagic telangiectasia*
SMARCA4: *Rhabdoid tumor predisposition syndrome, Coffin-Siris syndrome*
SMARCB1: *Rhabdoid tumor predisposition syndrome, Schwannomatosis, Coffin-Siris syndrome*
STK11: *Peutz-Jeghers syndrome*
SUFU: *Gorlin syndrome, Basal cell nevus syndrome*
TMEM127: *Hereditary paraganglioma-pheochromocytoma syndrome*
TP53: *Li-Fraumeni syndrome*
TSC1: *Tuberous sclerosis complex*
TSC2: *Tuberous sclerosis complex*
VHL: *Von Hippel-Lindau syndrome*
WT1: *WT1 Disorder*

[§] Special reporting – *EPCAM*: Large deletions only; *POLD1*: Exonuclease domain only; *POLE*: Exonuclease domain only.