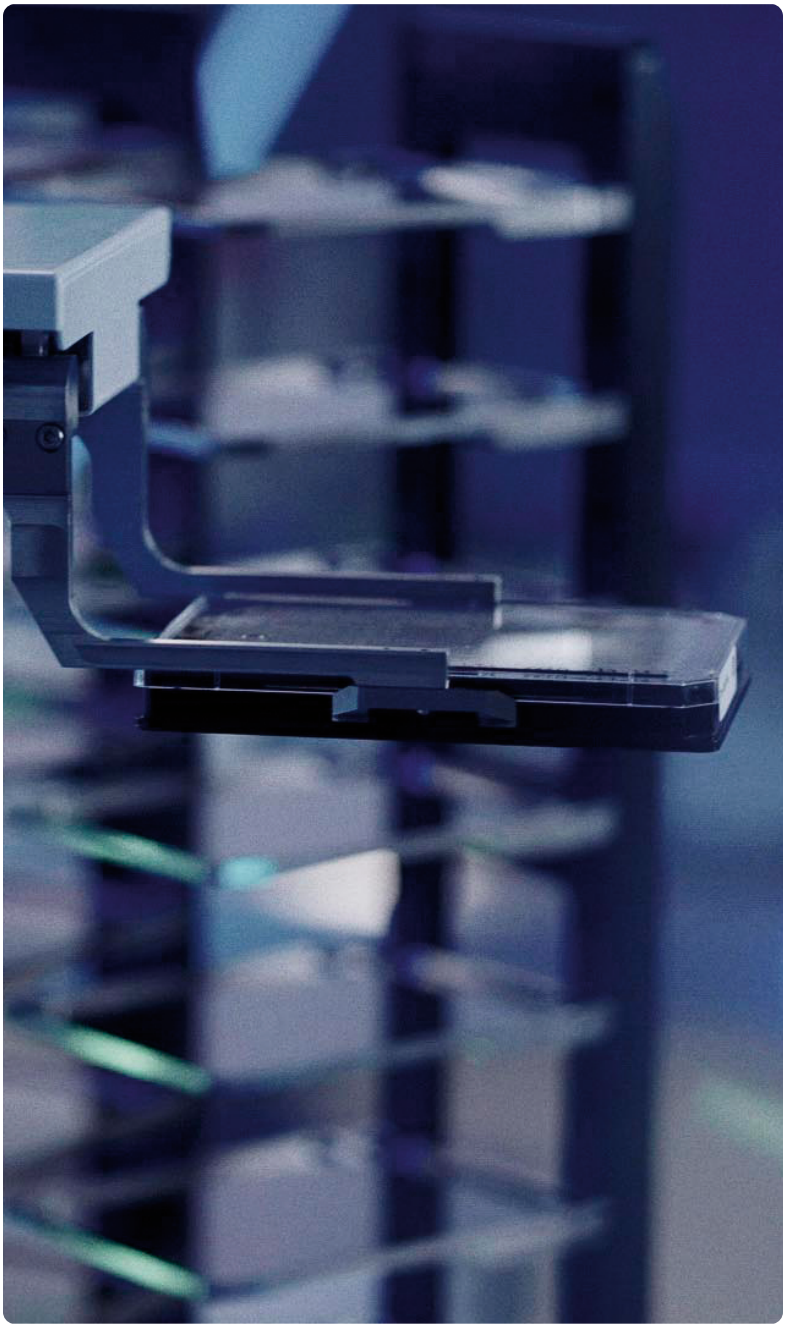
TEMPUS | ONCOLOGY

Germline Assay Guide



This is data-driven precision medicine.
This is the future of healthcare.

tempus.com/oncology/

Validated Hereditary Cancer Testing

(powered by Ambry Genetics®)

CancerNext-*Expanded*®

77-gene hereditary cancer DNA test, powered by Ambry Genetics®.

CancerNext®

40-gene hereditary cancer DNA test, powered by Ambry Genetics®.

+RNAinsight®

Optional add-on for CancerNext® or CancerNext-*Expanded*® that analyzes RNA to support the classification and detection of DNA variants, powered by Ambry Genetics®.

BRCAplus®

A guideline-based, disease-specific test option that includes 13 genes associated with hereditary breast cancer, where screening, treatment, and/or surgical intervention may be indicated. Can be ordered as a standalone test or in addition to CancerNext® or CancerNext-*Expanded*®.

xT CDx Solid Tumor + Normal Match

FDA-approved 648-gene tissue-based NGS test for molecular profiling of all malignant solid tumors, including companion diagnostic (CDx) claims for colorectal cancer (CRC) patients. Leveraging a tumor + normal matched approach, xT CDx identifies somatic variants unique to the tumor by filtering out germline variants from the normal match.

Tempus Professional Services

Based on the xT CDx normal match, potential germline findings from a select list of 63 hereditary cancer genes may be reported in the professional services report.

What are the differences between validated hereditary cancer testing and xT CDx tumor + normal match testing?

Hereditary Testing

CancerNext®/CancerNext-*Expanded*® and BRCAplus® are stand-alone validated germline tests that identify various types of germline alterations, including single and multi-exon deletions/duplications and gene rearrangements, depending on the genes assessed.

CancerNext®/CancerNext-*Expanded*® and BRCAplus® are specifically designed to provide hereditary cancer risk assessment and as such, sensitivity and specificity have been rigorously assessed.

Potential germline reporting in the professional services report of xT CDx tumor + normal matched testing assists in the identification of patients who may benefit from confirmatory follow-up testing with hereditary cancer testing.

	Validated Hereditary Cancer Testing *(powered by Ambry Genetics®)*	Tempus Professional Services xT CDx Tumor + Normal Match (Potential Germline)
Genes Assessed	CancerNext®: 40-gene guidelines-based germline panel that includes genes associated with hereditary breast, ovarian, pancreatic, prostate, colorectal, endometrial, gastric, small bowel, urothelial, and renal cancers. CancerNext-*Expanded*®: 77-gene germline panel that includes genes associated with hereditary breast, ovarian, pancreatic, prostate, colorectal, endometrial, gastric, small bowel, urothelial, renal, plus an array of additional cancers. BRCAplus®: Focused hereditary breast cancer panel assessing 13 clinically actionable genes with established management and treatment implications.	63 hereditary cancer genes
Types of Variants Detected	Single nucleotide variants (SNVs), Insertion and deletion alterations (indels), large deletions/duplications, rearrangements/inversions	SNVs, INDELS
Possible Results Included on Report	Pathogenic variants, likely pathogenic variants, variants of uncertain significance (VUS)	Pathogenic variants, likely pathogenic variants (available in the professional services report)
Validation	Rigorous validation process for hereditary cancer risk assessment	Validated for somatic testing; no specific hereditary validation
Secondary Confirmation	Performed for regions of inadequate NGS sequencing coverage (Sanger seq, MLPA, targeted chromosomal microarray)	Not performed
RNA Analysis	+RNAinsight® is an optional add-on for CancerNext® or CancerNext-*Expanded*®, that analyzes RNA to support the classification and detection of DNA variants.	Tempus xR can be ordered as a standalone or with xT CDx, offering full transcriptome RNA analysis for unbiased fusion and select splice variants detection. xR is a tissue based assay and is not utilized in germline classification or reporting.
Sample Types Accepted	Blood, Saliva, Cultured Fibroblasts*	Normal match: Blood, Saliva
Familial Variant/ Cascade Testing	Available for pathogenic/likely pathogenic variants	Not available
Variant Reclassification	Ambry Genetics® reclassifies; amendments issued through Tempus	Not available
Therapeutic Implications	Not included on report	The professional services report highlights information for clinicians to consider on biomarker-associated matches to FDA-approved therapies and therapeutic insights using MSK's OncoKB™ and NCCN Guidelines®
Patient Genetic Counseling Services	Available with ordering provider referral	Not available

**Requires Skin Punch Biopsy specimen kit and dedicated requisition.*
The reportable findings for the genes included on the above panels are based upon recommendations from the ACMG, the NCCN, and/or other published literature. The clinical significance of reported variants are based on germline classification criteria created by the American College of Medical Genetics (ACMG) and Association for Molecular Pathology (AMP).

CancerNext® / CancerNext-Expanded® and +RNAinsight®, powered by Ambry Genetics® is available to select providers.

xT CDx is a qualitative Next Generation Sequencing (NGS)-based in vitro diagnostic device intended for use in the detection of substitutions (single nucleotide variants (SNVs) and multi-nucleotide variants (MNVs)) and insertion and deletion alterations (INDELs) in 648 genes, as well as microsatellite instability (MSI) status, using DNA isolated from Formalin-Fixed Paraffin Embedded (FFPE) tumor tissue specimens, and DNA isolated from matched normal blood or saliva specimens, from previously diagnosed cancer patients with solid malignant neoplasms.The test is intended as a companion diagnostic (CDx) to identify patients who may benefit from treatment with the targeted therapies listed in the Companion Diagnostic Indications table in accordance with the approved therapeutic product labeling. Additionally, xT CDx is intended to provide tumor mutation profiling to be used by qualified health care professionals in accordance with professional guidelines in oncology for patients with previously diagnosed solid malignant neoplasms. Genomic findings other than those listed in the Companion Diagnostic Indications table are not prescriptive or conclusive for labeled use of any specific therapeutic product. xT CDx is a single-site assay performed at Tempus AI, Inc., Chicago, IL. For the complete xT CDx label, including companion diagnostic indications and important risk information, please visit tempus.com/xt-cdx-label/