xF Liquid Biopsy – 105 genes

Tsuei Lian Ke

Reported date : Aug 30, 2023

Tsuei Lian Ke

Diagnosis
Malignant neoplasm of pancreas

Accession No.
TL-23-H8BFFRCQ

xF

Date of Birth
09/25/1950

Sex
Female

Physician
Li-Yuan Bai

Institution
China Medical University Hospital
12357270

TEMPUS | xF
105 gene liquid biopsy

cfDNA specimen:
Peripheral Blood
Collected 8/21/2023
Received 8/24/2023

GENOMIC VARIANTS

Biologically Relevant		Variant Allele Fraction
NF1	c.7869+1G>A Splice region variant - LOF	0.4%

Median Variant Allele Fraction

0.4%

IMMUNOTHERAPY MARKERS

Microsatellite Instability Status

MSI-High not detected

TREATMENT IMPLICATIONS

No reportable treatment options found.

CLINICAL TRIALS

PF-07284892 in Participants With Advanced Solid Tumors (NCT04800822)	**Phase I** Grand Rapids, MI - 130 mi ✓ **NF1 c.7869+1G>A mutation**
Tovorafenib (DAY101) Monotherapy or in Combination With Other Therapies for Patients With Melanoma and Other Solid Tumors (NCT04985604)	**Phase I/II** Indianapolis, IN - 159 mi ✓ **NF1 c.7869+1G>A mutation**
A Basket Trial of an ERK1/2 Inhibitor (LY3214996) in Combination With Abemaciclib. (NCT04534283)	**Phase II** Indianapolis, IN - 164 mi ✓ **NF1 c.7869+1G>A mutation**

VARIANTS OF UNKNOWN SIGNIFICANCE

Gene	Mutation effect	Variant allele fraction
ARID1A	c.547G>A p.A183T Missense variant NM_006015	50.9%
NF1	c.1007G>T p.W336L Missense variant NM_001042492	0.9%

LOW COVERAGE REGIONS

ERRFI1	JAK1	KMT2A	MSH3	SPOP	TERT

VARIANT DETAILS - BIOLOGICALLY RELEVANT

NF1 c.7869+1G>A NM_001042492 Splice region variant - LOF VAF: 0.4%

NF1 is a tumor suppressor that plays a role in cellular growth and differentiation through the regulation of the Ras protein. Loss of function mutations and copy number loss of NF1 are associated with cancer progression.

Assay Description

The Tempus xF assay is a next-generation sequencing (NGS) cell-free DNA liquid biopsy tumor profiling assay for identifying genomic alterations derived from solid tumors but circulating in the blood. The 105 gene panel includes single nucleotide variants (SNVs), insertions and deletions (indels), copy number variants (CNVs) and chromosomal rearrangements (translocations) detected by hybrid capture NGS using custom designed IDT probes. The assay typically uses 30 to 50 ng of input DNA, and at 30 ng of input material, the technical sensitivity is >99% for SNVs and CNV amplifications at ≥0.5% variant allele fraction (VAF), and >98% for indels and >97% for translocations at >0.5% VAF. The assay spans clinically relevant coding exons for 35 genes and covers recurrent hotspot mutations in 70 genes. Insertions and deletions will be reported down to the lower limit of detection (LLOD) in clinically relevant regions in 97 genes (list available upon request). BRCA1 and BRCA2 copy number losses are reported when detected. At the discretion of the attending pathologists, the assay may be run at 10 to <30 ng of input DNA, but in such a case, the report will indicate reduced sensitivity and consideration should be given to additional testing. Please see the Tempus website for a complete gene list and performance specifications.

Potentially Actionable alterations are protein-altering variants with an associated therapy, diagnostic, and/or prognostic indication, based on evidence from clinical guidelines and medical literature. **Biologically Relevant** variants have functional significance or an association with the disease state in the medical literature, but do not have relevant therapeutic, prognostic or diagnostic evidence in the Tempus knowledge database. **Variants of Unknown Significance (VUSs)** exhibit an unclear effect on function and/or do not have sufficient evidence to determine their pathogenicity. **Benign variants** are not reported. **Low Coverage Regions** are included when mean coverage over any region(s) of a gene falls below a threshold of 1000x. The absence of alterations in genes with low coverage should be interpreted carefully in the context of the patient's diagnosis with consideration for retesting. Variants are identified through aligning the patient's DNA sequence to the human genome reference sequence version hg19 (GRCh37). The clinical summary shows actionable and biologically relevant variants. Because sequencing is performed without a matched normal sample, it is not possible to distinguish whether reported variants are germline or somatic.

Microsatellite instability (MSI) refers to hypermutability caused by genetic or acquired defects in the DNA mismatch repair pathway. **MSI-high (MSI-H)** tumors have changes in microsatellite repeat lengths due to defective DNA mismatch repair activity. MSI-H status is reported when detected. If MSI status will affect clinical management, immunohistochemical staining for DNA mismatch repair proteins, or another method of ascertaining MSI status, is recommended.

xF provides insights into the clinically relevant biomarkers incorporated in OncoKB, NCCN and other oncology guidelines for:

Bladder cancer: FGFR2, FGFR3

Breast cancer: BRCA1, BRCA2, ERBB2 (HER2), ESR1, PIK3CA

Cholangiocarcinoma:FGFR2, IDH1

Colorectal cancer: BRAF, ERBB2 (HER2), KRAS, NRAS

Assay Description (continued)

Gastroesophageal adenocarcinoma: ERBB2 (HER2)

Gastrointestinal stromal tumor: KIT, PDGFRA

Melanoma: BRAF, KIT, NRAS

Non-small cell lung cancer: ALK, BRAF, EGFR, ERBB2 (HER2), KRAS, MET, RET, ROS1

Complete Gene List

A-C
AKT1, AKT2, ALK, APC, AR, ARAF, ARID1A, ATM, ATR, B2M, BAP1, BRAF, BRCA1, BRCA2, BTK, CCND1, CCND2, CCND3, CCNE1, CD274 (PD-L1), CDH1, CDK4, CDK6, CDKN2A, CTNNB1

D-F
DDR2, DPYD, EGFR, ERBB2 (HER2), ERRFI1, ESR1, EZH2, FBXW7, FGFR1, FGFR2, FGFR3, FGFR4, FLT3, FOXL2

G-M
GATA3, GNA11, GNAQ, GNAS, HNF1A, HRAS, IDH1, IDH2, JAK1, JAK2, JAK3, KDR, KEAP1, KIT, KMT2A, KRAS, MAP2K1, MAP2K2, MAPK1, MET, MLH1, MPL, MSH2, MSH3, MSH6, MTOR, MYC, MYCN

N-R
NF1, NF2, NFE2L2, NOTCH1, NPM1, NRAS, NTRK1, PALB2, PBRM1, PDCD1LG2, PDGFRA, PDGFRB, PIK3CA, PIK3R1, PMS2, PTCH1, PTEN, PTPN11, RAD51C, RAF1, RB1, RET, RHEB, RHOA, RIT1, RNF43, ROS1

S-Z
SDHA, SMAD4, SMO, SPOP, STK11, TERT, TP53, TSC1, TSC2, UGT1A1, VHL

Gene Rearrangements
ALK, BRAF, FGFR2, FGFR3, NTRK1, RET, ROS1

Copy Number Gains
CCNE1, CD274 (PD-L1), EGFR, ERBB2 (HER2), MET, MYC

Copy Number Losses
BRCA1 and BRCA2

Tempus Disclaimer

The analysis of nucleic acids by next-generation sequencing (NGS) can be affected by multiple factors including DNA quality, hemolysis of the peripheral blood sample, and low amounts of circulating cell-free DNA limiting sensitivity. Tempus may report findings below our sensitivity threshold due to reduced sample quality and/or quantity. For samples flagged as falling below this threshold, Tempus advises resequencing in order to provide more accurate results. Additionally, the chance of detecting genetic alterations may be reduced in regions of the genome which are structurally difficult to sequence, in homologous genes, or due to sequencing errors.

Genetic alterations are defined as clinically significant based on peer-reviewed published literature and other authoritative sources such as NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). These references are not comprehensive, therefore clinically unknown findings may occur.

These test results and information contained within the report are current as of the report date. Tempus will not update reports or send notification regarding reclassification of genomic alterations. This test was developed and its performance characteristics determined by Tempus Labs, Inc. It has not been cleared or approved by the US Food and Drug Administration. The laboratory is CLIA certified to perform high-complexity testing. Any decisions related to patient care and treatment choices should be based on the independent judgment of the treating physician and should take into account all information related to the patient, including without limitation, the patient and family history, direct physical examination and other tests. Tempus is not liable for medical judgment with regards to diagnosis, prognosis or treatment in connection with the test results.

Note that certain tumor type-, sample- or variant-related characteristics, such as low cell-free DNA concentration, may result in reduced analytic sensitivity of the xF test for detection of alterations in the covered genes, including the above mentioned guideline-recommended genes.

Dostarlimab is indicated for the treatment of patients with mismatch repair deficient (dMMR) endometrial cancer or solid tumors. Although patients with MSI-H cancers are likely dMMR, confirmatory testing is recommended.

Tempus Disclaimer (continued)

Dates and times are represented in the coordinated universal time zone (UTC) unless otherwise specified. However, dates that are provided to Tempus without a timestamp (e.g., sample collection date) are listed as provided.

This assay cannot distinguish whether cell-free variants detected in plasma are derived from a patient's solid tumor or from clonal blood cells. Variants associated with clonal hematopoietic processes may be detected in a high percentage of older individuals and are especially common in the following genes:

ATM, BRAF, BRCA1, BRCA2, EZH2, FLT3, GNAS, IDH1, IDH2, JAK2, KIT, KRAS, NOTCH1, NPM1, NRAS, PALB2, PTPN11, RAD51C, RHOA, TP53

Correlation with tumor and/or blood sequencing results may be helpful in clarifying the origin of variants in some cases.

1. Genovese G, Kahler AK, Handsaker RE, et al. Clonal hematopoiesis and blood-cancer risk inferred from blood DNA sequence. N Engl J Med. 2014;371:2477-2487.

2. Jaiswal S, Fontanillas P, Flannick J, et al. Age-related clonal hematopoiesis associated with adverse outcomes. N Engl J Med. 2014;371:2488-2498.

3. Chan HT, Chin YM, Nakamura Y, et al. Clonal Hematopoiesis in Liquid Biopsy: From Biological Noise to Valuable Clinical Implications. Cancers 2020, 12, 2277. https://doi.org/10.3390/cancers12082277

A non-invasive, liquid biopsy panel of 105 genes focused on oncogenic and resistance mutations in cell-free DNA (cfDNA). This panel is designed to provide clinical decision support for solid tumors.

- SNVs (single nucleotide variants) and insertions and deletions (indels) are detected in all 105 genes
- Copy Number Amplifications (CNAs), Copy Number Deletions (CNDs)[1], and gene rearrangements (translocations) are detected in a subset of genes
- DNA Sequencing Depth: average 20,000x (raw reads)/5,000x (unique reads)
- Specimen Requirements: Two Streck tubes of peripheral blood (8.5mL each)

The report includes genomic alterations in select genes, microsatellite instability status[2], median variant allele fraction (mVAF), therapy options and clinical trials matched to the patient's genomic profile, as well as clinical history.

xF GENE PANEL

AKT1	BRAF	CDK6	FGFR1	HRAS	MAP2K1	MYCN	PDGFRA	RET	TERT
AKT2	BRCA1	CDKN2A	FGFR2	IDH1	MAP2K2	NF1	PDGFRB	RHEB	TP53
ALK	BRCA2	CTNNB1	FGFR3	IDH2	MAPK1	NF2	PIK3CA	RHOA	TSC1
APC	BTK	DDR2	FGFR4	JAK1	MET	NFE2L2	PIK3R1	RIT1	TSC2
AR	CCND1	DPYD	FLT3	JAK2	MLH1	NOTCH1	PMS2	RNF43	UGT1A1
ARAF	CCND2	EGFR	FOXL2	JAK3	MPL	NPM1	PTCH1	ROS1	VHL
ARID1A	CCND3	ERBB2 (HER2)	GATA3	KDR	MSH2	NRAS	PTEN	SDHA	
ATM	CCNE1	ERRFI1	GNA11	KEAP1	MSH3	NTRK1	PTPN11	SMAD4	
ATR	CD274 (PD-L1)	ESR1	GNAQ	KIT	MSH6	PALB2	RAD51C	SMO	
B2M	CDH1	EZH2	GNAS	KMT2A	MTOR	PBRM1	RAF1	SPOP	
BAP1	CDK4	FBXW7	HNF1A	KRAS	MYC	PDCD1LG2	RB1	STK11	

GENE REARRANGEMENTS

ALK	BRAF	FGFR2	FGFR3	NTRK1	RET	ROS1

COPY NUMBER GAINS

CCNE1	CD274 (PD-L1)	EGFR	ERBB2 (HER2)	MET	MYC

COPY NUMBER LOSSES

BRCA1	BRCA2

PERFORMANCE SPECIFICATIONS

	Variant Allele Fraction (VAF)	Sensitivity[3]
Single Nucleotide Variants (SNV)	>0.5% 0.50% 0.25% 0.10%[4]	>99.9% >99.9% 97% 70.4%
Insertions and Deletions	>0.5% 0.50% 0.25%	98.8% 96.0% 81.0%
Copy Number Amplifications (CNAs)	>0.5% 0.5%	>99.9% >99.9%
Rearrangements/ Fusions	>0.5% 0.50%	97.4% 70.8%

ANALYTICAL SPECIFICITY

Variant Type	Specificity[3]
SNV	>99.9%
INDEL	>99.9%
CNA	96.2%
Fusion	>99.9%

1. BRCA1 and BRCA2 copy number loss are reported when detected
2. MSI status will be reported when the specimen is determined to be MSI-High
3. Established using reference materials
4. For selected hot spot regions

xFGeneList_092120

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xF Validation

The non-invasive Tempus xF liquid biopsy assay detects cell-free DNA (cfDNA) in blood specimens of advanced solid tumor patients. The assay is capable of detecting mutations in two variant classes in ~105 genes, including: Single Nucleotide Variants (SNVs) and insertions and deletions (indels), as well as Copy Number Amplifications (CNAs) in 6 genes, Copy Number Deletions (CNDs) in 2 genes*, and gene rearrangements (translocations) in 7 genes spanning ~0.3 Mb of genomic space. The assay spans clinically relevant coding exons for 24 genes and covers recurrent hotspot mutations in 70 genes. Insertions and deletions will be reported down to the lower limit of detection (LLOD) in clinically relevant regions in 97 genes (list available upon request). Microsatellite Instability High (MSI-H) status is also reported when detected. The panel is designed to provide clinical decision support for patients with solid tumors and is focused on the identification of oncologic, including resistance, mutations.

CAP/CLIA validation of the Tempus xF panel focused on the detection of actionable oncologic and resistance variants in blood plasma. The assay requires two 8.5 mL Streck tubes of peripheral blood. Clinical sequencing is performed to ~20,000x coverage (at least 5,000x deduplicated reads). Performance specifications are listed in Table 1 below. These results establish, as shown in the table, high sensitivity and specificity for the Tempus xF assay.

Not intended for:

- Hematologic malignancies
- Early stage (stage I/II) cancers
- Primary CNS malignancies

TABLE 1: PERFORMANCE SPECIFICATIONS

Variant Class	Variant Allele Fraction (VAF)	Sensitivity	Specificity
Single Nucleotide Variants (SNVs)	>0.50%	>99.9%	>99.9%
	0.50%	>99.9%	>99.9%
	0.25%	97.0%	>99.9%
	0.10%	70.4%	>99.9%
Insertions and Deletions	>0.50%	98.8%	>99.9%
	0.50%	96.0%	>99.9%
	0.25%	81.0%	>99.9%
Copy Number Amplifications (CNAs)	>0.50%	>99.9%	96.2%
	0.50%	>99.9%	96.2%
Rearrangements/Fusions	>0.50%	97.4%	>99.9%
	0.50%	70.8%	>99.9%
Microsatellite Instability High (MSI-H) Status	N/A	37.5%	>99.9%

** BRCA1 and BRCA2 copy number loss are reported when detected*

TEMPUS

Data-driven Precision Medicine

Using modern genomic sequencing and state-of-the-art technology, we connect physicians with up-to-date treatment options and relevant insights that can be immediately translated into patient care.

SPECIMEN GUIDELINES

xT **Solid tumor** tissue collection

- Patient material, labeled with two identifiers
- Tumor samples should be from the most recent procedure, if adequate for testing.
- FFPE Fixation Requirements:
  - 10% formalin fixation (neutral buffered) for 6-72 hours, paraffin embedded
  - No decalcification of the samples (EDTA decalcification is accepted)
- Tumor is required to be at least 20% (40% for xE panel) of the sample by ratio of tumor nuclei to benign nuclei.
- Optimal tumor size = 25 mm², minimum = 5 mm²

BLOCKS *Preferred collection method

1 FFPE block with greatest tumor content

1 H&E stained slide, optional

If you would like us to evaluate quality, please send multiple blocks with a return address.

OR

SLIDES

10 FFPE unstained slides for NGS 5µm sections on positively charged, unbaked slides

1 Terminal H&E stained slide

6 FFPE unstained slides when DNA mismatch repair protein panel IHC is ordered

3 FFPE unstained slides when PD-L1 IHC is ordered

*** Submit 10 additional slides if tissue size is < 25 mm²*

COLLECTION INSTRUCTIONS

xT **Matched normal** or xF **Liquid biopsy** blood collection

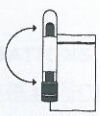
1. 

*repeat with second tube

Complete both specimen identification labels and affix one to each tube as shown.

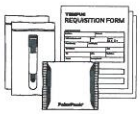
Collect 8.5 mL of blood in each provided blood tube using your institution's standard venipuncture technique.

Ensure the tubes are at room temperature prior to use.

2. 

*repeat with second tube

Immediately after drawing blood, mix by gently inverting the tube 8 to 10 times. Seal each blood tube into its own biohazard bag.

3. 

Place both sealed blood tube bags into the foam in the collection kit box along with the provided unfrozen polar pack, requisition form, and accompanying documents.

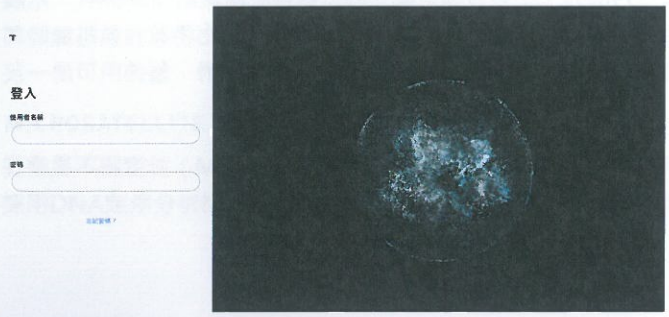
SENDING SAMPLES

Send via priority shipping using the packaging included in the Tempus collection kit.
Attention: Tempus Labs | 600 West Chicago Ave, Suite 510 | Chicago, IL 60654

TEMPUS 基因定序專有名詞解釋

Tempus 報告

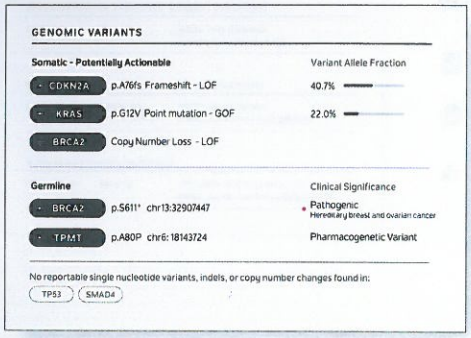
當Tempus收到腫瘤標本，會對樣本進行檢測分析，大約2-3週後醫生會收到為每個患者準備的完整全面報告，重點突出關鍵發現，包括潛在可行的治療方法、免疫療法標誌物和匹配的臨床試驗。以下是報告中可能包含的專有名詞的解釋說明。



PDF檔案使用容易解說與理解的排版，適合醫師和病人共同閱讀和討論。另外提供TEMPUS專業版HUB，僅開放給醫師註冊使用。https://accounts.securetempus.com/

- **可排序和設定條件篩選全部報告列表**
- **可連結到ClinicalTrials.gov臨床試驗數據庫**
- **跟免疫治療相關的科學資訊(研究用途、僅限xT檢測才有)**
- **可直接與TEMPUS Medical Affairs進行Case Review**

基因變異



當我們發現癌細胞裡的DNA變異，就稱它為「體細胞基因變異」，是癌症發生的原因。有些「體細胞基因變異」可以有標靶藥物，但不是所有基因變異都有標靶藥物，原因可能是：1.突變位點並非用藥對應位點、2.或是藥物還在臨床試驗階段、3.或是藥物還在研發階段。

體細胞 潛在可行動的變異

如果這個基因變異有標靶藥物或療法，可以減緩或阻止癌細胞的生長和擴散，或縮小腫瘤，或是可搭配其他藥物提高治療效果；或是已知會讓某種標靶藥物產生抗藥性，那麼這個基因變異就被定義是「潛在可行動的變異」

體細胞 生物學相關的變異

如果這個基因變異，以目前的科學能力尚未開發出可治療的藥物，那麼這個基因變異就定義是「生物學相關的變異」

生殖細胞變異 **僅限 xT 檢測才有**

這些是跟遺傳有關的突變，有的跟罹癌風險有關，有的跟美國醫學遺傳學和基因學院（ACMG）所列表之「醫學上可採取行動的」的基因有關

MUTATIONS 突變

突變是基因DNA序列的變化，可以是在體細胞（後天性得到的）或生殖細胞（先天遺傳的）。此外，對於每個體細胞突變，Tempus提供變異等位基因比例（VAF），即定序檢體中基因組變異的讀取比例，以百分比表示。

COPY NUMBER VARIATIONS (CNV) 拷貝數變異

基因拷貝數變異報告有2種：包括擴增（拷貝數增加）或缺失（拷貝數減少）報告。Tempus透過DNA定序檢測CNV。若是失去雜合性（LOH）失去兩個編碼等位基因中的一個，也會在報告中註明。

CHROMOSOMAL REARRANGEMENTS (TRANSLOCATIONS) 染色體重組（易位）

染色體結構重組是指兩個分開的基因片段重組在一起形成融合基因。融合基因可能會產生異常和/或過度活躍的蛋白質，進而導致腫瘤生成、進展或抗藥性。Tempus 採用兩種序列檢測方法檢測重組（易位）：對部分基因進行 DNA 序列檢測，以及對全轉錄組 RNA 序列進行融合分析(RNA融合分析僅限xT檢測才有)。

TEMPUS 基因定序專有名詞解釋

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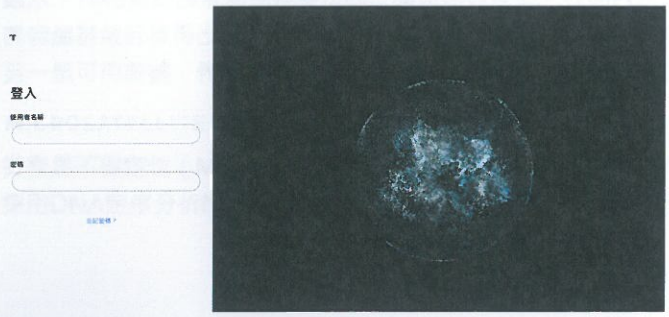

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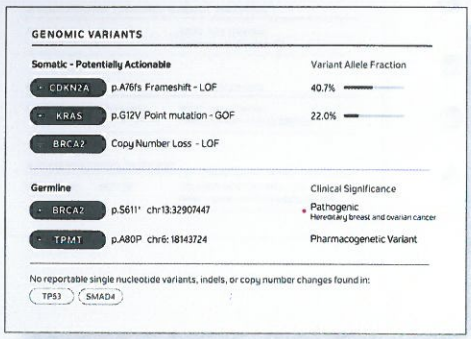

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如果這個基因變異有標靶藥物或療法，可以減緩或阻止癌細胞的生長和擴散，或縮小腫瘤，或是可搭配其他藥物提高治療效果；或是已知會讓某種標靶藥物產生抗藥性，那麼這個基因變異就被定義是「潛在可行動的變異」

體細胞生物學相關的變異

如果這個基因變異，以目前的科學能力尚未開發出可治療的藥物，那麼這個基因變異就定義是「生物學相關的變異」

生殖細胞變異 **僅限 xT 檢測才有**

這些是跟遺傳有關的突變，有的跟罹癌風險有關，有的跟美國醫學遺傳學和基因學院（ACMG）所列表之「醫學上可採取行動的」的基因有關

MUTATIONS 突變

突變是基因DNA序列的變化，可以是在體細胞（後天性得到的）或生殖細胞（先天遺傳的）。此外，對於每個體細胞突變，Tempus提供變異等位基因比例（VAF），即定序檢體中基因組變異的讀取比例，以百分比表示。

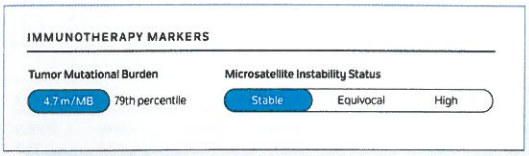
COPY NUMBER VARIATIONS (CNV) 拷貝數變異

基因拷貝數變異報告有2種：包括擴增（拷貝數增加）或缺失（拷貝數減少）報告。Tempus透過DNA定序檢測CNV。若是失去雜合性（LOH）失去兩個編碼等位基因中的一個，也會在報告中註明。

CHROMOSOMAL REARRANGEMENTS (TRANSLOCATIONS) 染色體重組（易位）

染色體結構重組是指兩個分開的基因片段重組在一起形成融合基因。融合基因可能會產生異常和/或過度活躍的蛋白質，進而導致腫瘤生成、進展或抗藥性。Tempus 採用兩種序列檢測方法檢測重組（易位）：對部分基因進行 DNA 序列檢測，以及對全轉錄組 RNA 序列進行融合分析(RNA融合分析僅限xT檢測才有)。

免疫治療生物標記



檢測免疫治療的關鍵生物標記，包括微衛星不穩定狀態（MSI）、腫瘤突變負荷（TMB），以及 PD-L1 和 MMR錯配修復(PD-L1 和MMR是選購項目，若無選購則無此報告)

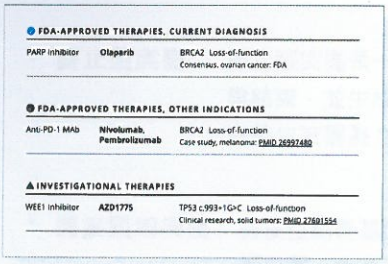
TUMOR MUTATIONAL BURDEN (TMB) 腫瘤突變負荷量

腫瘤突變負荷（TMB）是一個衡量腫瘤中攜帶的突變數量的數值，即每百萬個鹼基對中改變蛋白質的體細胞突變的數量。研究顯示，TMB高的腫瘤對免疫療法的反應可能性增加。TEMPUS 的TMB報告是通過將非同義突變數量除以TEMPUS Panel的每百萬個鹼基數計算得出的。將 TMB 大於等於10 定義為 “高” 。除了TMB原始分數（mut/Mb），TMB百分位數是報告中提供的另一個可用數據，代表檢測樣本的TMB分數在整個Tempus癌數據庫中的排名。

MICROSATELLITE INSTABILITY (MSI) 微衛星不穩定性

微衛星不穩定性（MSI）狀態是指因DNA錯配修復受損而導致的基因組不穩定性，是一種免疫治療生物標記物參考。Tempus採用DNA定序分析MSI狀態(也可選購IHC-MMR)。微衛星不穩定性-高 (MSI-H) 代表與對免疫療法反應的可能性增加有關。

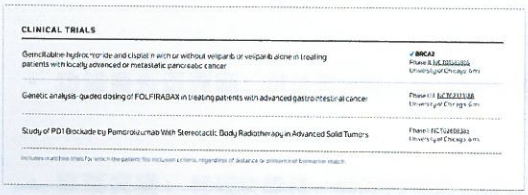
治療意義



根據這次送檢的腫瘤基因分析報告，提出有醫學證據的治療方法

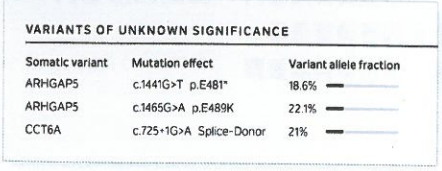
- ✓ 美國FDA核可療法，適用目前診斷
- ✓ 美國FDA核可療法，其他適應症
- ▲ 研究性療法是指正在進行臨床試驗研究和評估，尚未被監管機構批准使用的醫療方法。臨床試驗階段確定其安全性、有效性、劑量和潛在的副作用。研究性療法通常被使用在已用盡所有可用治療方案，或用於那些患有罕見或難以治療的疾病的病人。參加研究性療法臨床試驗的病人由醫療服務提供者密切監測，以評估該療法的潛在益處和風險。

臨床試驗



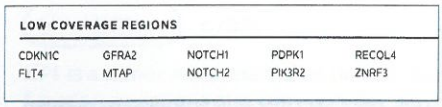
根據此次送檢的腫瘤基因特徵以及癌症類型和臨床病史，TEMPUS為您配對了一份最新的臨床試驗清單

意義不明的變異



意義不明的體細胞變異（VUS）是指這個DNA變異與癌症生物學有關的證據還不夠充分或證據還不夠明確。為了避免與 "生物相關 "和 "臨床可操作 "混淆，TEMPUS不會報告意義不明的變異（VUSs）的基因變異。

低覆蓋區域

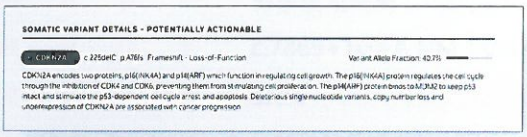


LOW COVERAGE REGIONS

CDKN1C	GFRA2	NOTCH1	PDPK1	RECQL4
FLT4	MTAP	NOTCH2	PIK3R2	ZNRF3

低覆蓋率區域是指基因被定序的深度或質量低於實驗室的閥值規定。由於技術限制或其他因素，某個區域沒能以符合實驗室規定的深度或質量被定序。低覆蓋率區域會使得基因變異鑑定變得困難，所以若確實有變異也可能無法被檢測出。

變異詳細說明



SOMATIC VARIANT DETAILS - POTENTIALLY ACTIONABLE

CDKN2A c.225delC p.A76fs Frameshift - Loss-of-Function Variant Allele Fraction: 42.7%

CDKN2A encodes two proteins, p16(INK4A) and p14(ARF) which function in regulating cell growth. The p16(INK4A) protein regulates the cell cycle through the inhibition of CDK4 and CDK6, preventing them from stimulating cell proliferation. The p14(ARF) protein binds to MDM2 to keep p53 intact and stimulate the p53-dependent cell cycle arrest and apoptosis. Deleterious single nucleotide variants, copy number loss and underexpression of CDKN2A are associated with cancer progression

Tempus採用次世代定序檢測體細胞可操作和生物相關的基因組變異和/或偶然發現的生殖細胞突變。 Tempus的報告總結了檢測到的基因變異，包括變異位置、影響和基因功能。

- **錯義突變：** 錯義突變是一種可能發生在我們DNA中的變化。我們的基因是由DNA組成的，DNA包含構建我們身體正常運作所需的所有蛋白質的指令。當DNA編碼指令的一個代碼發生變化時，就會發生錯義突變，進而導致產生不同的氨基酸，進而影響蛋白質的功能，這種改變可能導致疾病或根本沒有影響。錯義變體是否有害取決於許多因素，如變化的位置和它影響的蛋白質的重要性。

- **終止型突變：** 終止型突變是一種發生在基因中的突變，這種突變導致了一個終止密碼子的產生，它會讓蛋白質合成提早結束，並生成為一個斷掉不完整的蛋白質，這個蛋白質通常是無功能或功能障礙的。這種類型的突變有時也被稱為 無義突變或過早終止密碼子突變。

- **剪接區域突變：** 剪接位點是基因的特定區域，在這裡DNA序列被切割並粘貼在一起，以形成最終的mRNA，用於構建蛋白質。這個過程被稱為剪接。然而，如果剪接位點出現突變，剪接過程可能出錯，基因的外顯子（編碼區）可能無法正確地剪接在一起。其結果是往往是一個外顯子被排除在之外，這可能導致產生一種異常的蛋白質或根本沒有蛋白質。

- **功能獲得型突變：** 用於描述導致蛋白質具有增強或新功能的基因變化。當一個突變改變了一個基因的DNA序列，導致其編碼的蛋白質變得更有活性、或是出現新的功能。

- **功能喪失型突變：** 導致蛋白質失去正常功能的DNA序列變化。

- **移碼突變：** 移碼突變是一種基因突變，通常是由於基因序列中的插入或刪除等錯誤而導致的，會改變蛋白質翻譯的讀框架，從而使其產生不同的氨基酸序列，並可能導致蛋白質合成的提前終止。通常會導致蛋白質喪失正常功能。

- **內部缺失突變：** 內部缺失突變是基因突變的一種，其中一小段 DNA 缺失(通常是3個或3的倍數)，這會導致基因的錯誤拼接，但是整個基因依然能夠翻譯成一個功能性的蛋白質。換言之，可以想像成是拼圖少了一塊，但是整張圖還是能夠看出來。這種突變通常會影響基因的功能，有時也會和癌症的發生有關。

TEMPUS 基因變異詳細說明-中英對照

中文翻譯僅供參考，非正式報告

VARIANT DETAILS - BIOLOGICALLY RELEVANT

NF1 c.7869+1G>A NM_001042492 Splice region variant - LOF VAF: 0.4%

NF1 is a tumor suppressor that plays a role in cellular growth and differentiation through the regulation of the Ras protein. Loss of function mutations and copy number loss of NF1 are associated with cancer progression.

中文翻譯僅供參考，非正式報告

基因名稱：NF1

變異種類：剪接區域突變、功能喪失型突變

變異位點：c.7869+1G>A NM_001042492

變異等位基因比例：0.4%

基因功能解釋：NF1基因是我們DNA的一部分，它含有製造一種特殊蛋白質的指令。這種蛋白質有助於控制另一種蛋白質並參與細胞生長和分裂過程。當NF1基因正常運作時，會形成一種天然防禦機制防止癌症發生，透過調節來防止細胞不受控制地生長。然而，當NF1基因存在問題，例如基因突變或缺失時，會使細胞無法受到控制地生長和分裂，從而導致癌症的發生。(英文原譯: NF1是一種腫瘤抑制因子，透過調節Ras蛋白質在細胞生長和分化方面發揮作用。NF1的功能缺失突變和拷貝數缺失與癌症進展有關)。

檢測名稱：TEMPUS xF 液態切片癌症基因檢測

項目類別	類別說明	結果
基因組變異：	潛在可行的變異	未發現可報告的致病變異。
	生物學相關的變異	NF1 c.7869+1G>A Splice region variant - LOF Variant Allele Fraction: 0.4%
免疫治療標誌：	微衛星不穩定狀態	高度微衛星不穩定未檢出。
治療意義：	無	未發現可報告的治療選項。

臨床試驗	根據此次送檢的腫瘤基因特徵以及癌症類型所配對最新的臨床試驗清單

臨床試驗編號：NCT04800822
試驗目的：評估藥物PF-07284892對於患有晚期實體腫瘤的受試者的效果。
試驗階段：一期
地點：位於美國
基因焦點：NF1基因的c.7869+1G>A突變

臨床試驗編號：NCT04985604
試驗目的：研究藥物Tovorafenib（也稱為DAY101）在單獨使用或與其他治療方法結合治療黑色素瘤和其他實體腫瘤患者的效果。
試驗階段：一/二期
地點：美國
基因焦點：NF1基因的c.7869+1G>A突變

臨床試驗編號：NCT04534283
試驗目的：評估ERK1/2抑制劑LY3214996與Abemaciclib聯合治療對於患有NF1基因c.7869+1G>A突變的受試者的效果。
試驗階段：二期
地點：位於美國
基因焦點：NF1基因的c.7869+1G>A突變

請注意，以上資訊僅供參考，詳細的試驗資訊和參與資格請與試驗負責單位聯繫以獲得最準確的資訊。

意義不明的變異:		
基因名稱	突變說明	異常等位基因比例
ARID1A	c.547G>A p.A183T Missense variant NM_006015	50.9 %

NF1	c.1007G>T p.W336L Missense variant NM_001042492	0.9%

低覆蓋區域
ERRFI1、JAK1、KMT2A、MSH3、SPOP、TERT

檢測敘述
Tempus xF檢測是一種次世代定序的cfDNA液體活檢腫瘤分析檢測，用於檢測從固體腫瘤中釋放到血液中的基因變異。這105基因檢測包括有單核苷酸變異（SNV）、插入與刪除（indels）、拷貝數變異（CNV）和染色體重排（易位），透過使用定制的IDT探針用於NGS混合捕獲進行偵測。該檢測通常使用30至50納克的輸入DNA，對於SNV和CNV放大，在≥0.5%的變異等位基因比例（VAF）以上之技術敏感性達到>99%，對於indels大於0.5%的VAF則達到>98%，對於易位大於0.5%的VAF則達到>97%。該檢測涵蓋35個基因的臨床相關編碼外顯子，並包括70個基因中的重複熱點突變。達臨床相關區域的檢測下限（LLOD）的97個基因（可根據要求提供清單）之插入和刪除檢出會出報告。BRCA1和BRCA2的拷貝數減少檢出會出報告。在主治病理醫師的酌情下，檢測也可以使用10至<30納克的輸入DNA進行，但在這種情況下，報告將指出降低的敏感性，並應考慮進行其他測試。請參閱Tempus網站以獲取完整的基因列表和性能規範。 「潛在可行的變異」是指與特定治療、診斷和/或預後指示相關的影響蛋白質的變異，基於臨床指南和醫學文獻的證據。「生物相關的變異」在醫學文獻中具有功能意義或與疾病狀態有關，但在Tempus知識庫中沒有相關的治療、預後或診斷證據。「意義不明的變異」（VUS）對功能具有不明確的影響和/或缺乏足夠的證據來確定其致病性。不會報告良性變異。「低覆蓋區域」是指任何基因區域的平均覆蓋率低於1000倍時所包含的區域。在基因低覆蓋區域缺乏變異時，應謹慎解釋，並結合患者的診斷情況進行重新測試的考慮。通過將患者的DNA序列與人類基因組參考序列版本hg19（GRCh37）進行對比，可以識別出變異。臨床總結顯示了可行和與生物相關的變異。由於定序是在沒有相配對正常樣本的情況下進行的，無法區分報告的變異是體細胞遺傳的還是體細胞突變的。 「微衛星不穩定性（MSI）」是由於DNA錯配修復途徑的遺傳性或獲得性缺陷導致的高度突變性。MSI高（MSI-H）腫瘤由於DNA錯配修復活性缺陷而出現微衛星重複長度的變化。檢測到時會報告MSI-H狀態。如果MSI狀態將影響臨床管理，則建議進行DNA錯配修復蛋白的免疫組織化學染色，或採用其他方法確定MSI狀態。 xF提供了在OncoKB、NCCN和其他腫瘤學指南中包含的臨床相關生物標記物的訊息： 膀胱癌：FGFR2、FGFR3 乳腺癌：BRCA1、BRCA2、ERBB2（HER2）、ESR1、PIK3CA 膽管癌：FGFR2、IDH1 大腸直腸癌：BRAF、ERBB2（HER2）、KRAS、NRAS 胃食道腺癌：ERBB2（HER2） 胃腸道間質瘤：KIT、PDGFRA 黑色素瘤：BRAF、KIT、NRAS 非小細胞肺癌：ALK、BRAF、EGFR、ERBB2（HER2）、KRAS、MET、RET、ROS1 完整基因列表 A-C： AKT1、AKT2、ALK、APC、AR、ARAF、ARID1A、ATM、ATR、B2M、BAP1、BRAF、

BRCA1、BRCA2、BTK、CCND1、CCND2、CCND3、CCNE1、CD274（PD-L1）、CDH1、CDK4、CDK6、CDKN2A、CTNNB1
D-F：
DDR2、DPYD、EGFR、ERBB2（HER2）、ERRFI1、ESR1、EZH2、FBXW7、FGFR1、FGFR2、FGFR3、FGFR4、FLT3、FOXL2
G-M：
GATA3、GNA11、GNAQ、GNAS、HNF1A、HRAS、IDH1、IDH2、JAK1、JAK2、JAK3、KDR、KEAP1、KIT、KMT2A、KRAS、MAP2K1、MAP2K2、MAPK1、MET、MLH1、MPL、MSH2、MSH3、MSH6、MTOR、MYC、MYCNN-R
NF1、NF2、NFE2L2、NOTCH1、NPM1、NRAS、NTRK1、PALB2、PBRM1、PDCD1LG2、PDGFRA、PDGFRB、PIK3CA、PIK3R1、PMS2、PTCH1、PTEN、PTPN11、RAD51C、RAF1、RB1、RET、RHEB、RHOA、RIT1、RNF43、ROS1
S-Z：
SDHA、SMAD4、SMO、SPOP、STK11、TERT、TP53、TSC1、TSC2、UGT1A1、VHL
基因重排：
ALK、BRAF、FGFR2、FGFR3、NTRK1、RET、ROS1
拷貝數增加：
CCNE1、CD274（PD-L1）、EGFR、ERBB2（HER2）、MET、MYC
拷貝數缺失：
BRCA1 和 BRCA2

*中文翻譯僅供參考，非正式報告

檢測收據

No. S230831

受檢者姓名	出生日期	經辦者	收據日期
柯翠蓮 Tsuei Lian Ke	1950 年 9 月 25 日	陳愛蓉	112/08/31
依醫師診斷，治療期間因病情需要，委外進行基因檢測。			

檢測項目	廠牌	金額
xF 液態切片癌症基因檢測-105 genes	TEMPUS	NT$90,000
合計		NT$90,000

信息者基因有限公司收據章

信息者基因有限公司 統一編號 69409967 TEL:02-2649-0599 新北市汐止區大同路一段499號10樓之2

QA 38084326

統一發票（二聯式）

一一二年七、八月份

中華民國 112 年 8 月 31 日

買受人：柯翠蓮

地址：縣市 鄉鎮市區 路街 段 巷 弄 號 樓 室

品名	數量	單價	金額	備註
基因檢測	1	90000	90000	
				營業人蓋用統一發票專用章
總計			90000	

總計新臺幣（中文大寫）億 仟 佰 拾 二萬 仟 佰 拾 元

課稅別 應稅 ✓ 零稅率 免稅

信息者基因有限公司 統一發票專用章 統一編號 69409967 新北市 汐止區 大同路一段499號10樓之2

※應稅、零稅率、免稅之銷售額應分別開立統一發票，並應於各該欄打「✓」。

第二聯 收執聯