楊光瑞
Project ID: C23-M001-02052
Report No.: AA-23-04365_ONC
Date Reported: Jul 17, 2023

# ACT Onco® + Report

| PATIENT | | |
|---|---|---|
| Identifier: 楊光瑞 | | Patient ID: 40202571 |
| Date of Birth: Mar 12, 1969 | | Gender: Male |
| Diagnosis: Lung adenocarcinoma | | |
| **ORDERING PHYSICIAN** | | |
| Name: 趙恒勝醫師 | | Tel: 886-228712121 |
| Facility: 臺北榮總 | | |
| Address: 臺北市北投區石牌路二段 201 號 | | |
| **SPECIMEN** | | |
| Specimen ID: S11229881A | Collection site: Lung | Type: FFPE tissue |
| Date received: Jul 04, 2023 | Lab ID: AA-23-04365 | D/ID: NA |

**ABOUT ACTOnco®+**

The test is a next-generation sequencing (NGS)-based assay developed for efficient and comprehensive genomic profiling of cancers. This test interrogates coding regions of 440 genes associated with cancer treatment, prognosis and diagnosis. Genetic mutations detected by this test include small-scale mutations like single nucleotide variants (SNVs), small insertions and deletions (InDels) (≤ 15 nucleotides) and large-scale genomic alterations like copy number alterations (CNAs). The test also includes an RNA test, detecting fusion transcripts of 13 genes.

## SUMMARY FOR ACTIONABLE VARIANTS

### VARIANTS/BIOMARKERS WITH EVIDENCE OF CLINICAL SIGNIFICANCE

| Genomic Alterations/Biomarkers | Probable Effects in Patient's Cancer Type | | Probable Sensitive in Other Cancer Types |
|---|---|---|---|
| | Sensitive | Resistant | |
| Not detected | | | |

### VARIANTS/BIOMARKERS WITH POTENTIAL CLINICAL SIGNIFICANCE

| Genomic Alterations/Biomarkers | Possibly Sensitive | Possibly Resistant |
|---|---|---|
| SMARCA4 E579* | Tazemetostat | - |

**Note:**

- The above summary tables present genomic variants and biomarkers based on the three-tiered approach proposed by US FDA for reporting tumor profiling NGS testing. "Variants/biomarkers with evidence of clinical significance" refers to mutations that are widely recognized as standard-of-care biomarkers (FDA level 2/AMP tier 1). "Variants/biomarkers with potential clinical significance" refers to mutations that are not included in the standard of care but are informational for clinicians, which are commonly biomarkers used as inclusion criterial for clinical trials (FDA level 3/AMP tier 2).
- The therapeutic agents and possible effects to a given drug are based on mapping the variants/biomarkers with ACT Genomics clinical knowledge database. The mapping results only provide information for reference, but not medical recommendation.
- Please refer to corresponding sections for more detailed information about genomic alteration and clinical relevance listed above.

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## TESTING RESULTS

### VARIANT(S) WITH CLINICAL RELEVANCE

#### - Single Nucleotide and Small InDel Variants

| Gene | Amino Acid Change | Allele Frequency |
|---|---|---|
| *SMARCA4* | E579* | 11.5% |
| *TP53* | Splice acceptor | 9.2% |

#### - Copy Number Alterations

| Chromosome | Gene | Variation | Copy Number |
|---|---|---|---|
| Chr11 | *MUC6* | Homozygous deletion | 0 |

#### - Fusions

| Fusion Gene & Exon | Transcript ID |
|---|---|
| No fusion gene detected in this sample | |

#### - Immune Checkpoint Inhibitor (ICI) Related Biomarkers

| Biomarker | Results |
|---|---|
| Tumor Mutational Burden (TMB) | 3.2 muts/Mb |
| Microsatellite Instability (MSI) | Microsatellite stable (MSS) |

Note:
- Variant(s) enlisted in the SNV table may currently exhibit no relevance to treatment response prediction. Please refer to INTERPRETATION for more biological information and/or potential clinical impacts of the variants.
- Loss of heterozygosity (LOH) information was used to infer tumor cellularity. Copy number alteration in the tumor was determined based on 30% tumor purity.
- TMB was calculated by using the sequenced regions of ACTOnco®+ to estimate the number of somatic nonsynonymous mutations per megabase of all protein-coding genes (whole exome). The threshold for high mutation load is set at ≥ 7.5 mutations per megabase. TMB, microsatellite status and gene copy number deletion cannot be determined if calculated tumor purity is < 30%.

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## THERAPEUTIC IMPLICATIONS

### TARGETED THERAPIES

| Genomic Alterations | Therapies | Effect |
|---|---|---|
| **Level 3B** | | |
| ***SMARCA4*** E579* | Tazemetostat | **sensitive** |

Therapies associated with benefit or lack of benefit are based on biomarkers detected in this tumor and published evidence in professional guidelines or peer-reviewed journals.

| Level | Description |
|---|---|
| 1 | FDA-recognized biomarkers predictive of response or resistance to FDA approved drugs in this indication |
| 2 | Standard care biomarkers (recommended by the NCCN guideline) predictive of response or resistance to FDA approved drugs in this indication |
| 3A | Biomarkers predictive of response or resistance to therapies approved by the FDA or NCCN guideline in a different cancer type |
| 3B | Biomarkers that serve as inclusion criteria for clinical trials (minimal supportive data required) |
| 4 | Biomarkers that show plausible therapeutic significance based on small studies, few case reports, or preclinical studies |

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## IMMUNE CHECKPOINT INHIBITORS (ICIs)

No genomic alterations detected to confer sensitivity or lack of benefit to immune checkpoint therapies.

## - Other Biomarkers with Potential Clinical Effects for ICIs

| Genomic Alterations | Potential Clinical Effects |
|---|---|
| Not detected | |

Note: Tumor non-genomic factors, such as patient germline genetics, PDL1 expression, tumor microenvironment, epigenetic alterations or other factors not provided by this test may affect ICI response.

## CHEMOTHERAPIES

| Genomic Alterations | Therapies | Effect | Level of Evidence | Cancer Type |
|---|---|---|---|---|
| ***SMARCA4*** E579* | Cisplatin, Vinorelbine | **Sensitive** | Clinical | Lung cancer |
| | Cyclophosphamide, Doxorubicin | **Less sensitive** | Clinical | Breast cancer |

## HORMONAL THERAPIES

No genomic alterations detected in this tumor predicted to confer sensitivity or lack of benefit to hormonal therapies.

## OTHERS

No genomic alterations detected in this tumor predicted to confer sensitivity or lack of benefit to other therapies.

**Note:**
Therapeutic implications provided in the test are based solely on the panel of 440 genes sequenced. Therefore, alterations in genes not covered in this panel, epigenetic and post-transcriptional and post-translational factors may also determine a patient's response to therapies. In addition, several other patient-associated clinical factors, including but not limited to, prior lines of therapies received, dosage and combinations with other therapeutic agents, patient's cancer types, sub-types, and/or stages, may also determine the patient's clinical response to therapies.

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## VARIANT INTERPRETATION

### *SMARCA4* E579*

#### Biological Impact

The SWI/SNF-related, matrix-associated, actin-dependent regulator of chromatin, subfamily a, member 4 (SMARCA4) gene encodes an ATP-dependent helicase, a catalytic subunit of the SWI/SNF chromatin remodeling complex which play a role in gene transcription, DNA synthesis and DNA repair[1][2][3]. SMARCA4 has been implicated as a haploinsufficient gene as demonstrated by the development of mammary tumors in SMARCA4 heterozygous mice[4]. SMARCA4 is the most frequently mutated gene among the SWI/SNF subunits and its inactivation bas been implicated in malignant rhabdoid tumors, lymphoma, medulloblastoma, lung and ovarian cancer[5][6][7]. Germline mutations in the SMARCA4 gene predispose carriers to pediatric atypical teratoid/ rhabdoid tumors (AT/RT)[6][7][8]and small cell carcinoma of the ovary of hypercalcemic type (SCCOHT)[9][10][11].

E579* mutation results in a premature truncation of the SMARCA4 protein at amino acid 579 (UniProtKB). This mutation is predicted to lead to a loss of SMARCA4 function, despite not having been characterized in the literature.

#### Therapeutic and prognostic relevance

Results of in vitro and in vivo preclinical models showed that SMARCA2- and SMARCA4-deficient small-cell carcinoma of the ovary hypercalcemic type (SCCOHT) were sensitive to the inhibitor of the H3K27 histone methyltransferase (EZH2), tazemetostat[12]. Clinical trials are underway to evaluate the efficacy of tazemetostat in patients with SMARCA4 loss or mutation (NCT03155620, NCT03213665, and NCT02601950).

Low SMARCA4 expression is a significant prognostic biomarker to predict increased sensitivity to cisplatin and vinorelbine combination chemotherapy in non-small cell lung cancer (NSCLC) patients[13]. Loss or reduced expression of SMARCA4 and SMARCB1 in triple-negative breast cancer (TNBC) cell lines and patients correlated with poor response to doxorubicin-containing regimen (doxorubicin and cyclophosphamide)[14].

### *TP53* Splice acceptor

#### Biological Impact

TP53 encodes the p53 protein, a crucial tumor suppressor that orchestrates essential cellular processes including cell cycle arrest, senescence and apoptosis[15]. TP53 is a proto-typical haploinsufficient gene, such that loss of a single copy of TP53 can result in tumor formation[16].

TP53 c.673-1G>T is a variant located at the splice acceptor region, which may result in the exon skipping.

#### Therapeutic and prognostic relevance

Despite having a high mutation rate in cancers, there are currently no approved targeted therapies for TP53 mutations. A phase II trial demonstrated that Wee1 inhibitor (AZD1775) in combination with carboplatin was well tolerated and showed promising anti-tumor activity in TP53-mutated ovarian cancer refractory or resistant (< 3 months) to standard first-line therapy (NCT01164995)[17].

In a retrospective study (n=19), advanced sarcoma patients with TP53 loss-of-function mutations displayed improved progression-free survival (208 days versus 136 days) relative to patients with wild-type TP53 when treated with pazopanib[18]. Results from another Phase I trial of advanced solid tumors (n=78) demonstrated that TP53 hotspot mutations are associated with better clinical response to the combination of pazopanib and vorinostat[19].

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Advanced solid tumor and colorectal cancer patients harboring a TP53 mutation have been shown to be more sensitive to bevacizumab when compared with patients harboring wild-type TP53[20][21][22]. In a pilot trial (n=21), TP53-negative breast cancer patients demonstrated increased survival following treatment with bevacizumab in combination with chemotherapy agents, Adriamycin (doxorubicin) and Taxotere (docetaxel)[23]. TP53 mutations were correlated with poor survival of advanced breast cancer patients receiving tamoxifen or primary chemotherapy[24][25]. In a retrospective study of non-small cell lung cancer (NSCLC), TP53 mutations were associated with high expression of VEGF-A, the primary target of bevacizumab, offering a mechanistic explanation for why patients exhibit improved outcomes after bevacizumab treatment when their tumors harbor mutant TP53 versus wild-type TP53[26].

## *MUC6* Homozygous deletion

### Biological Impact

MUC6 encodes a secretory mucin glycoprotein that is physiologically expressed in the digestive tract. Abnormal MUC6 expression has been found in various human cancers arising in the stomach, duodenum, breast, pancreas, endometrium, colorectum and lung[27]. Overexpression of MUC6 has been shown to inhibit tumor proliferation and invasion in vitro[28][29]. In Wilms tumor, MUC6 overexpression suppresses the expression of β-catenin and its target genes via autophagy-dependent mechanism, while MUC6 knock-down leads to the opposite effects, supporting a possible tumor suppressor role[29].

### Therapeutic and prognostic relevance

Lack of MUC6 expression was associated with shorter overall survival in patients with well- to moderately-differentiated gallbladder cancer[30]. MUC6-expressing pulmonary invasive mucinous adenocarcinoma demonstrated superior survival to MUC6-negative cases[31]. In colorectal cancer, high MUC6 expression was associated with improved progression-free and cancer-specific survival[32].

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## US FDA-APPROVED DRUG(S)

### Tazemetostat (TAZVERIK)

Tazemetostat is an inhibitor of the methyltransferase, EZH2, and some EZH2 gain-of-function mutations including Y646X, A682G, and A692V. Tazemetostat is developed and marketed by Epizyme under the trade name TAZVERIK.

### - FDA Approval Summary of Tazemetostat (TAZVERIK)

| | |
|---|---|
| **E7438-G000-101**<br>NCT01897571 | **Follicular lymphoma** (Approved on 2020/06/18) |
| | **EZH2 mutation** |
| | Tazemetostat (ezh2 mutant) vs. Tazemetostat (ezh2 wild-type) [ORR(%): 69.0 vs. 34.0, DOR(M): 10.9 vs. 13] |
| **EZH-202**<br>NCT02601950 | **Epithelioid sarcoma** (Approved on 2020/01/23) |
| | **INI1 loss** |
| | Tazemetostat [ORR(%): 15.0] |

D=day; W=week; M=month

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## ONGOING CLINICAL TRIALS

Trials were searched by applying filters: study status, patient's diagnosis, intervention, location and/or biomarker(s). Please visit https://clinicaltrials.gov to search and view for a complete list of open available and updated matched trials.

No trial has been found.

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## SUPPLEMENTARY INFORMATION OF TESTING RESULTS

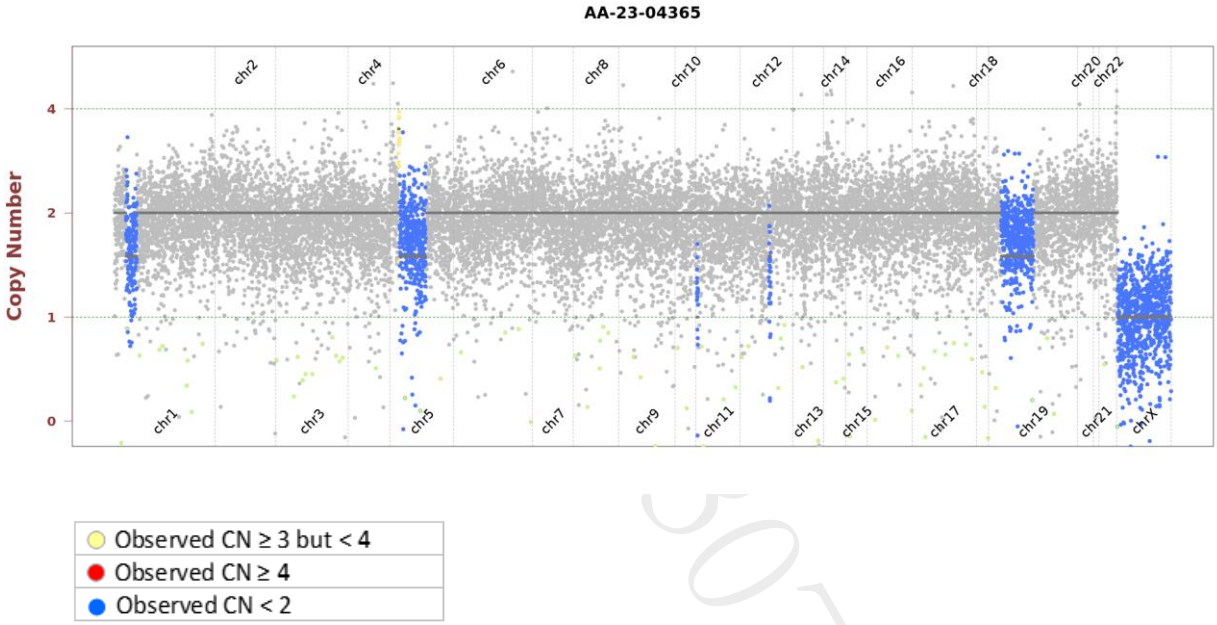
### DETAILED INFORMATION OF VARIANTS WITH CLINICAL RELEVANCE

#### - Single Nucleotide and Small InDel Variants

| Gene | Amino Acid Change | Exon | cDNA Change | Accession Number | COSMIC ID | Allele Frequency | Coverage |
|---|---|---|---|---|---|---|---|
| SMARCA4 | E579* | 11 | c.1735G>T | NM_001128844 | - | 11.5% | 434 |
| TP53 | Splice acceptor | - | c.673-1G>T | NM_000546 | COSM45135 | 9.2% | 1300 |

#### - Copy Number Alterations

Observed copy number (CN) for each evaluated position is shown on the y-axis. Regions referred to as amplification or deletion are shown in color. Regions without significant changes are represented in gray.



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## OTHER DETECTED VARIANTS

| Gene | Amino Acid Change | Exon | cDNA Change | Accession Number | COSMIC ID | Allele Frequency | Coverage |
|---|---|---|---|---|---|---|---|
| AKT1 | Splice region | - | c.287+5G>A | NM_005163 | - | 51.1% | 562 |
| AKT3 | Q78H | 3 | c.234G>T | NM_005465 | - | 12.8% | 549 |
| ARID2 | T938S | 15 | c.2813C>G | NM_152641 | COSM7346274 | 53.3% | 1230 |
| EPHA2 | G489V | 7 | c.1466G>T | NM_004431 | - | 49.1% | 230 |
| ESR2 | L413V | 8 | c.1237C>G | NM_001437 | COSM7637015 | 44.8% | 747 |
| HIF1A | Q347E | 9 | c.1039C>G | NM_001530 | - | 53.0% | 812 |
| IKBKE | Splice region | - | c.813-4G>A | NM_014002 | COSM7274319 | 56.4% | 1147 |
| KDR | D1241N | 28 | c.3721G>A | NM_002253 | - | 45.0% | 458 |
| MUC16 | T3567S | 3 | c.10700C>G | NM_024690 | - | 55.4% | 720 |
| MUC4 | A864S | 2 | c.2590G>T | NM_018406 | - | 47.5% | 1056 |
| PRKDC | G769D | 21 | c.2306G>A | NM_006904 | COSM454625 | 9.6% | 1144 |
| PTCH1 | A741V | 14 | c.2222C>T | NM_000264 | - | 42.4% | 2152 |
| USH2A | P4735Q | 65 | c.14204C>A | NM_206933 | - | 7.0% | 981 |

Note:

- This table enlists variants detected by the panel other than those with clinical relevance (reported in Testing Result section). The clinical impact of a genetic variant is determined according to ACT Genomics in-house clinical knowledge database. A negative result does not necessarily indicate absence of biological effect on the tumor. Some variants listed here may possibly have preclinical data or may show potential clinical relevance in the future.

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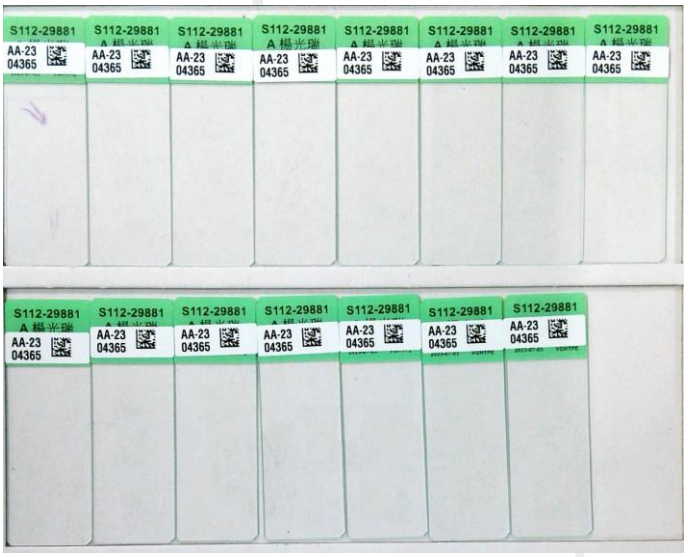
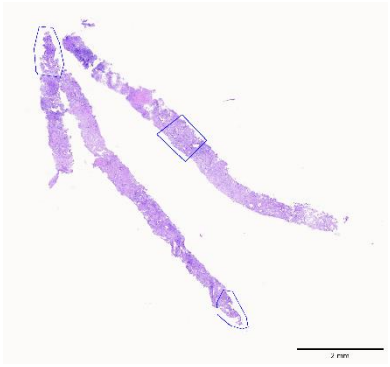
## TEST DETAILS

### SPECIMEN RECEIVED AND PATHOLOGY REVIEW



- Collection date: Jun 21, 2023
- Facility retrieved: 臺北榮總
- H&E-stained section No.: S11229881A
- Collection site: Lung
- Examined by: Dr. Yun-An Chen
    1. The percentage of viable tumor cells in total cells in the whole slide (%): 5%
    2. The percentage of viable tumor cells in total cells in the encircled areas in the whole slide (%): 40%
    3. The percentage of necrotic cells (including necrotic tumor cells) in total cells in the whole slide (%): 0%
    4. The percentage of necrotic cells (including necrotic tumor cells) in total cells in the encircled areas in the whole slide (%): 0%
    5. Additional comment: NA
- Manual macrodissection: Performed on the highlighted region
- The outline highlights the area of malignant neoplasm annotated by a pathologist.

### RUN QC

- Panel: ACTOnco®+

**DNA test**

- Mean Depth: 909x
- Target Base Coverage at 100x: 95%

**RNA test**

- Average unique RNA Start Sites per control GSP2: 84

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## LIMITATIONS

1. This test does not provide information of variant causality and does not detect variants in non-coding regions that could affect gene expression. This report does not report polymorphisms and we do not classify whether a mutation is germline or somatic. Variants identified by this assay were not subject to validation by Sanger or other technologies.
2. The possibility cannot be excluded that certain pathogenic variants detected by other sequencing tools may not be reported in the test because of technical limitation of bioinformatics algorithm or the NGS sequencing platform, e.g. low coverage.
3. This test has been designed to detect fusions in 13 genes sequenced. Therefore, fusion in genes not covered by this test would not be reported. For novel fusions detected in this test, Sanger sequencing confirmation is recommended if residue specimen is available.

## NEXT-GENERATION SEQUENCING (NGS) METHODS

**DNA test**

Extracted genomic DNA was amplified using primers targeting coding exons of analyzed genes and subjected to library construction. Barcoded libraries were subsequently conjugated with sequencing beads by emulsion PCR and enriched using Ion Chef system. Sequencing was performed according to Ion Proton or Ion S5 sequencer protocol (Thermo Fisher Scientific).

Raw reads generated by the sequencer were mapped to the hg19 reference genome using the Ion Torrent Suite. Coverage depth was calculated using Torrent Coverage Analysis plug-in. Single nucleotide variants (SNVs) and short insertions/deletions (InDels) were identified using the Torrent Variant Caller plug-in. VEP (Variant Effect Predictor) was used to annotate every variant using databases from Clinvar, COSMIC and Genome Aggregation database. Variants with coverage ≥ 20, allele frequency ≥ 5% and actionable variants with allele frequency ≥ 2% were retained. This test provides uniform coverage of the targeted regions, enabling target base coverage at 100x ≥ 85% with a mean coverage ≥ 500x.

Variants reported in Genome Aggregation database with > 1% minor allele frequency (MAF) were considered as polymorphisms. ACT Genomics in-house database was used to determine technical errors. Clinically actionable and biologically significant variants were determined based on the published medical literature.

The copy number alterations (CNAs) were predicted as described below:
Amplicons with read counts in the lowest 5th percentile of all detectable amplicons and amplicons with a coefficient of variation ≥ 0.3 were removed. The remaining amplicons were normalized to correct the pool design bias. ONCOCNV (an established method for calculating copy number aberrations in amplicon sequencing data by Boeva et al., 2014) was applied for the normalization of total amplicon number, amplicon GC content, amplicon length, and technology-related biases, followed by segmenting the sample with a gene-aware model. The method was used as well for establishing the baseline of copy number variations.

Tumor mutational burden (TMB) was calculated by using the sequenced regions of ACTOnco®+ to estimate the number of somatic nonsynonymous mutations per megabase of all protein-coding genes (whole exome). The TMB calculation predicted somatic variants and applied a machine learning model with a cancer hotspot correction. TMB may be reported as “TMB-High”, “TMB-Low” or “Cannot Be Determined”. TMB-High corresponds to ≥ 7.5 mutations per megabase (Muts/Mb); TMB-Low corresponds to < 7.5 Muts/Mb. TMB is reported as “Cannot Be Determined” if the tumor purity of the sample is < 30%.

Classification of microsatellite instability (MSI) status is determined by a machine learning prediction algorithm. The change of a number of repeats of different lengths from a pooled microsatellite stable (MSS) baseline in > 400 genomic loci are used as the features for the algorithm. The final output of the results is either microsatellite Stable (MSS) or microsatellite instability high (MSI-H).

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**RNA test**

Extracted RNA was reverse-transcribed and subjected to library construction. Sequencing was performed according to Ion Proton or Ion S5 sequencer protocol (Thermo Fisher Scientific). To ensure sequencing quality for fusion variant analysis, the average unique RNA Start Sites (SS) per control Gene Specific Primer 2 (GSP 2) should be ≥ 10.

The fusion analysis pipeline aligned sequenced reads to the human reference genome, identified regions that map to noncontiguous regions of the genome, applied filters to exclude probable false-positive events and, annotated previously characterized fusion events according to Quiver Gene Fusion Database, a curated database owned and maintained by ArcherDX. In general, samples with detectable fusions need to meet the following criteria: (1) Number of unique start sites (SS) for the GSP2 ≥ 3; (2) Number of supporting reads spanning the fusion junction ≥ 5; (3) Percentage of supporting reads spanning the fusion junction ≥ 10%; (4) Fusions annotated in Quiver Gene Fusion Database.

## DATABASE USED

- Reference genome: Human genome sequence hg19
- COSMIC v.92
- Genome Aggregation database r2.1.1
- ClinVar (version 20210404)
- ACT Genomics in-house database
- Quiver Gene Fusion Database version 5.1.18

**Variant Analysis:**
醫檢師黃靖婷 博士
Ching-Ting Huang Ph.D.
檢字第 016511 號

CT Huang

**Sign Off**
解剖病理專科醫師王業翰
Yeh-Han Wang M.D.
病解字第 000545 號

Yehn

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## GENE LIST

### SNV & CNV

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| ABCB1* | ABCC2* | ABCG2* | ABL1 | ABL2 | ADAMTS1 | ADAMTS13 | ADAMTS15 | ADAMTS16 | ADAMTS18 | ADAMTS6 | ADAMTS9 |
| ADAMTSL1 | ADGRA2 | ADH1C* | AKT1 | AKT2 | AKT3 | ALDH1A1* | ALK | AMER1 | APC | AR | ARAF |
| ARID1A | ARID1B | ARID2 | ASXL1 | ATM | ATR | ATRX | AURKA | AURKB | AXIN1 | AXIN2 | AXL |
| B2M | BAP1 | BARD1 | BCL10 | BCL2* | BCL2L1 | BCL2L2* | BCL6 | BCL9 | BCOR | BIRC2 | BIRC3 |
| BLM | BMPR1A | BRAF | BRCA1 | BRCA2 | BRD4 | BRIP1 | BTG1 | BTG2* | BTK | BUB1B | CALR |
| CANX | CARD11 | CASP8 | CBFB | CBL | CCNA1 | CCNA | CCNB1 | CCNB2 | CCNB3 | CCND1 | CCND2 |
| CCND3 | CCNE1 | CCNE2 | CCNH | CD19 | CD274 | CD58 | CD70* | CD79A | CD79B | CDC73 | CDH1 |
| CDK1 | CDK12 | CDK2 | CDK4 | CDK5 | CDK6 | CDK7 | CDK8 | CDK9 | CDKN1A | CDKN1B | CDKN2A |
| CDKN2B | CDKN2C | CEBPA* | CHEK1 | CHEK2 | CIC | CREBBP | CRKL | CRLF2 | CSF1R | CTCF | CTLA4 |
| CTNNA1 | CTNNB1 | CUL3 | CYLD | CYP1A1* | CYP2B6* | CYP2C19* | CYP2C8* | CYP2D6 | CYP2E1* | CYP3A4* | CYP3A5* |
| DAXX | DCUN1D1 | DDR2 | DICER1 | DNMT3A | DOT1L | DPYD | DTX1 | E2F3 | EGFR | EP300 | EPCAM |
| EPHA2 | EPHA3 | EPHA5 | EPHA7 | EPHB1 | ERBB2 | ERBB3 | ERBB4 | ERCC1 | ERCC2 | ERCC3 | ERCC4 |
| ERCC5 | ERG | ESR1 | ESR2 | ETV1 | ETV4 | EZH2 | FAM46C | FANCA | FANCC | FANCD2 | FANCE |
| FANCF | FANCG | FANCL | FAS | FAT1 | FBXW7 | FCGR2B | FGF1* | FGF10 | FGF14 | FGF19* | FGF23 |
| FGF3 | FGF4* | FGF6 | FGFR1 | FGFR2 | FGFR3 | FGFR4 | FH | FLCN | FLT1 | FLT3 | FLT4 |
| FOXL2* | FOXP1 | FRG1 | FUBP1 | GATA1 | GATA2 | GATA3 | GNA11 | GNA13 | GNAQ | GNAS | GREM1 |
| GRIN2A | GSK3B | GSTP1* | GSTT1* | HGF | HIF1A | HIST1H1C* | HIST1H1E* | HNF1A | HR | HRAS* | HSP90AA1 |
| HSP90AB1 | HSPA4 | HSPA5 | IDH1 | IDH2 | IFNL3* | IGF1 | IGF1R | IGF2 | IKBKB | IKBKE | IKZF1 |
| IL6 | IL7R | INPP4B | INSR | IRF4 | IRS1 | IRS2* | JAK1 | JAK2 | JAK3 | JUN* | KAT6A |
| KDM5A | KDM5C | KDM6A | KDR | KEAP1 | KIT | KMT2A | KMT2C | KMT2D | KRAS | LCK | LIG1 |
| LIG3 | LMO1 | LRP1B | LYN | MALT1 | MAP2K1 | MAP2K2 | MAP2K4 | MAP3K1 | MAP3K7 | MAPK1 | MAPK3 |
| MAX | MCL1 | MDM2 | MDM4 | MED12 | MEF2B | MEN1 | MET | MITF | MLH1 | MPL | MRE11 |
| MSH2 | MSH6 | MTHFR* | MTOR | MUC16 | MUC4 | MUC6 | MUTYH | MYC | MYCL | MYCN | MYD88 |
| NAT2* | NBN | NEFH | NF1 | NF2 | NFE2L2 | NFKB1 | NFKBIA | NKX2-1* | NOTCH1 | NOTCH2 | NOTCH3 |
| NOTCH4 | NPM1 | NQO1* | NRAS | NSD1 | NTRK1 | NTRK2 | NTRK3 | PAK3 | PALB2 | PARP1 | PAX5 |
| PAX8 | PBRM1 | PDCD1 | PDCD1LG2 | PDGFRA | PDGFRB | PDIA3 | PGF | PHOX2B* | PIK3C2B | PIK3C2G | PIK3C3 |
| PIK3CA | PIK3CB | PIK3CD | PIK3CG | PIK3R1 | PIK3R2 | PIK3R3 | PIM1 | PMS1 | PMS2 | POLB | POLD1 |
| POLE | PPARG | PPP2R1A | PRDM1 | PRKAR1A | PRKCA | PRKCB | PRKCG | PRKCI | PRKCQ | PRKDC | PRKN |
| PSMB8 | PSMB9 | PSME1 | PSME2 | PSME3 | PTCH1 | PTEN | PTGS2 | PTPN11 | PTPRD | PTPRT | RAC1 |
| RAD50 | RAD51 | RAD51B | RAD51C | RAD51D | RAD52 | RAD54L | RAF1 | RARA | RB1 | RBM10 | RECQL4 |
| REL | RET | RHOA | RICTOR | RNF43 | ROS1 | RPPH1 | RPTOR | RUNX1 | RUNX1T1 | RXRA | SDHA |
| SDHB | SDHC | SDHD | SERPINB3 | SERPINB4 | SETD2 | SF3B1 | SGK1 | SH2D1A* | SLC19A1* | SLC22A2* | SLCO1B1* |
| SLCO1B3* | SMAD2 | SMAD3 | SMAD4 | SMARCA4 | SMARCB1 | SMO | SOCS1* | SOX2* | SOX9 | SPEN | SPOP |
| SRC | STAG2 | STAT3 | STK11 | SUFU | SYK | SYNE1 | TAF1 | TAP1 | TAP2 | TAPBP | TBX3 |
| TEK | TERT | TET1 | TET2 | TGFBR2 | TMSB4X* | TNF | TNFAIP3 | TNFRSF14 | TNFSF11 | TOP1 | TP53 |
| TPMT* | TSC1 | TSC2 | TSHR | TYMS | U2AF1 | UBE2A* | UBE2K | UBR5 | UGT1A1* | USH2A | VDR* |
| VEGFA | VEGFB | VHL | WT1 | XIAP | XPO1 | XRCC2 | ZNF217 | | | | |

*Analysis of copy number alterations NOT available.

### FUSION

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| ALK | BRAF | EGFR | FGFR1 | FGFR2 | FGFR3 | MET | NRG1 | NTRK1 | NTRK2 | NTRK3 | RET | ROS1 |

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# APPENDIX

## POSSIBLE THERAPEUTIC IMPLICATIONS FOR HETEROZYGOUS DELETION

Not Applicable.

## SIGNALING PATHWAYS AND MOLECULAR-TARGETED AGENTS

Not Applicable.

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## DISCLAIMER

### 法律聲明

本檢驗報告僅提供專業醫療參考，結果需經專業醫師解釋及判讀。基因突變資訊非必具備藥物或治療有效性指標，反之亦然。本檢驗報告提供之用藥指引不聲明或保證其臨床有效性，反之亦然。本基因檢測方法係由本公司研究開發，已經過有效性測試。
本檢驗報告非經本公司許可，不得私自變造、塗改，或以任何方式作為廣告及其他宣傳之用途。
本公司於提供檢驗報告後，即已完成本次契約義務，後續之報告解釋、判讀及用藥、治療，應自行尋求相關專業醫師協助，若需將報告移件其他醫師，本人應取得該醫師同意並填寫移件申請書，主動告知行動基因，行動基因僅能配合該醫師意願與時間提供醫師解說。

### 醫療決策需由醫師決定

任何治療與用藥需經由醫師在考慮病患所有健康狀況相關資訊包含健檢、其他檢測報告和病患意願後，依照該地區醫療照護標準由醫師獨立判斷。醫師不應僅依據單一報告結果(例如本檢測或本報告書內容)做決策。

### 基因突變與用藥資訊並非依照有效性排序

本報告中列出之生物標記變異與藥物資訊並非依照潛在治療有效性排序。

### 證據等級

藥物潛在臨床效益(或缺乏潛在臨床效益)的實證證據是依據至少一篇臨床療效個案報告或臨床前試驗做為評估。本公司盡力提供適時及準確之資料，但由於醫學科技之發展日新月異，本公司不就本報告提供的資料是否為準確、適宜或最新作保證。

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