# Thyroid Sample
# Timothy Strickland

Diagnosis
**Medullary thyroid cancer**

Accession No.
**7562**

xT

Date of Birth
**1979-01-19**

Sex
**Female**

Physician
**Dr. William Hays**

Institution
**Welch and Sons**

Tumor specimen:
source Thyroid
CollectedDate 2024-02-04
ReceivedDate 2024-02-06
TumorPercentage 77%

Normal specimen:
source Blood
CollectedDate 2024-02-05
ReceivedDate 2024-02-07

## GENOMIC VARIANTS

**Somatic - Potentially Actionable** — **variant allele fraction**

| | | |
|---|---|---|
| PTCH1 | c.3583A>T p.T1195S Missensevariant(exon2)-GOF | 18.3% |

**Somatic - Biologically Relevant**

| | | |
|---|---|---|
| XPC | c.3113A>G p.S346P Frameshift-GOF | 14.45% |
| PRKCA | c.1387G>C p.S346P Frameshift-GOF | 12.29% |

**Germline - Pathogenic**

No Germline - Pathogenic variants were found in the limited set of genes on which we report.

**Pertinent Negatives**

KIT NCSTN

## IMMUNOTHERAPY MARKERS

**Tumor Mutational Burden**

16 m/Mb 15%

**Microsatellite Instability Status**

Stable Equivocal **High**

## FDA-APPROVED THERAPIES, Current Diagnosis

| | | |
|---|---|---|
| KRAS G12C Inhibitors | **Sotorasib** | NCCN, Consensus, Non-Small Cell Lung Cancer<br>MSK OncoKB, Level 1<br>KRASp.G12C G12C-GOF |

## FDA-APPROVED THERAPIES, Other Indications

| | | |
|---|---|---|
| KRAS G12C Inhibitors | **Sotorasib** | NCCN, Consensus, Non-Small Cell Lung Cancer<br>MSK OncoKB, Level 1<br>KRASp.G12C G12C-GOF |

## ADDITIONAL INDICATORS

| | |
|---|---|
| **Unfavorable Prognosis** | NCCN, Consensus, Non-Small Cell Lung Cancer<br>KRASp.G12C Gain-of-function |

## CLINICAL TRIALS

| | |
|---|---|
| A Study of VS-6766 v. VS-6766 + Defactinib in Recurrent G12V, Other KRAS and BRAF Non-Small Cell Lung Cancer | **Phase 2**<br>City, state - x mi<br>**KRAS mutation** |
| A Phase 1/2 Study of MRTX849 in Patients With Cancer Having a KRAS G12C Mutation KRYSTAL-1 | **Phase 1/2**<br>City, state - x mi<br>**KRAS mutation**<br>**STK11 mutation** |
| First-in-human Study of DRP-104 (Sirpiglenastat) as Single Agent and in Combination With Atezolizumab in Patients With Advanced Solid Tumors. (NCT04471415) | **Phase 1/2**<br>City, state - x mi<br>**NFE2L2 mutation**<br>**STK11 mutation** |

## VARIANTS OF UNKNOWN SIGNIFICANCE

| **Somatic** | **Mutation effect** | **Variant allele fraction** |
|---|---|---|
| MYCN | c.131C>T p.P44L Frameshift-GOF<br>NM_001011645 | 25.0% |
| DICER1 | c.5437G>A p.D1810H Stopgain-LOF<br>NM_001011645 | 2.01% |
| TLR8 | c.3113A>G p.N515H Missensevariant(exon2)-GOF<br>NM_001011645 | 4.13% |
| MTOR | c.5664C>A p.G1954R Frameshift-LOF<br>NM_001011645 | 9.31% |
| ZEB2 | c.3113A>G p.H1038R Frameshift-GOF<br>NM_001011645 | 1.33% |
| ALDH2 | c.1510G>A p.E504K Nonsense-GOF<br>NM_001011645 | 2.46% |
| **Germline** | **Mutation effect** | **Condition** |
| MYCN | c.131_132delinsTT p.P44L Spliceregionvariant-LOF<br>NM_001011645 | myself |
| CTNNB1 | c.101G>T p.G34R Frameshift-LOF<br>NM_001011645 | choice |

## LOW COVERAGE REGIONS

TOP2A HBB NCSTN

## SOMATIC VARIANT DETAILS - POTENTIALLY ACTIONABLE

**PTCH1** c.3583A>T p.T1195S Missensevariant(exon2)-GOF VAF: 18.3%

FAT1 encodes a transmembrane protein involved in tumor suppressor signaling. FAT1 protein can regulate transcriptional activity by sequestering beta-catenin, thereby preventing it from entering the nucleus. Loss of function mutations and copy number loss of FAT1 are associated with cancer progression.

## SOMATIC VARIANT DETAILS - BIOLOGICALLY RELEVANT

**XPC** c.3113A>G p.S346P Frameshift-GOF VAF: 14.45%

ARID2 encodes a protein that is a subunit of the SWI/SNF chromatin remodeling complex SWI/SNF-B or PBAF. This complex functions in ligand-dependent transcriptional activation. Loss of function mutations and copy number loss of ARID2 are associated with cancer progression.

**PRKCA** c.1387G>C p.S346P Frameshift-GOF VAF: 12.29%

FAT1 encodes a transmembrane protein involved in tumor suppressor signaling. FAT1 protein can regulate transcriptional activity by sequestering beta-catenin, thereby preventing it from entering the nucleus. Loss of function mutations and copy number loss of FAT1 are associated with cancer progression.

## CLINICAL HISTORY

Diagnosed on

2024-02-03