Incidence of molecular alterations in *KRAS* and other known cancer genes in patients with pancreatic cancer assessed with a commercial genomic profiling panel compared to TCGA results

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INTRODUCTION

The Cancer Genome Atlas (TCGA) characterizes somatic mutations of pancreatic cancer (PC) patients using whole-exome sequencing (WES, mean coverage 405x) of fresh frozen tumor tissues and matched blood samples.

- Key genomic findings are confirmed by targeted sequencing (~644x) and microfluidic PCR-based sequencing (~30,000x)
- The vast majority of patients undergo genomic characterization of formalin-fixed, paraffin-embedded (FFPE) biopsy samples

In this study, we analyzed the detection rate of Tempus|xT gene alterations and biomarkers in PC FFPE samples and compared mutational frequencies with TCGA PC data.

METHODS

Matched tumor and normal specimens (peripheral blood or saliva) from 59 Baylor College of Medicine PC patients (Table 1) were sequenced using Tempus|xT, an LDT offering that includes a 648-gene DNA sequencing panel (coverage 500x), whole-transcriptome RNA sequencing (average depth of 50 million reads), and immunohistochemistry testing.

Retrospective analysis of detection rates of all clinically reported pathogenic mutations was performed using LENS, a proprietary application that allows for the interrogation and analysis of large de-identified molecular and clinical datasets.

RESULTS

Figure 1: Tempus|xT specimen and clinical results workflow

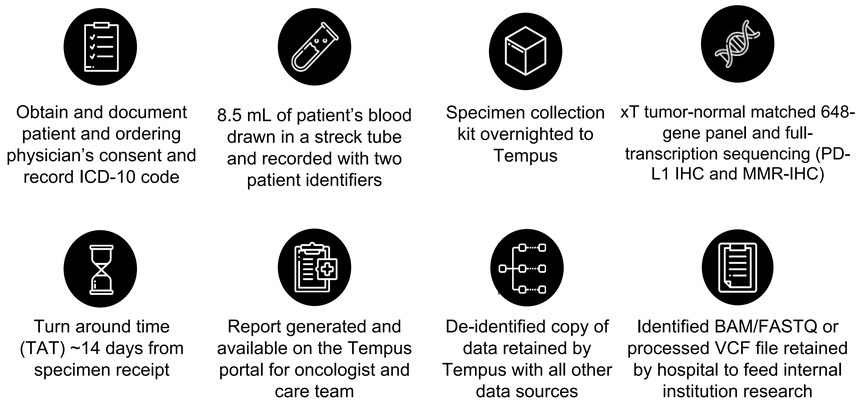

Figure 1. Following receipt of blood or tissue sample, the sample undergoes tumor-normal matched DNA sequencing and RNA sequencing. Generated reports are available on the Tempus portal for healthcare providers, a de-identified copy is retained by Tempus and raw data are returned to the institution.

Table 1: Clinical Characteristics

Total Patients	**n = 59**
Sex	
Female	30 (50.8%)
Male	29 (49.1%)
Age	
Median	67
Range	38-88
Tumor Percentage	
Median	30%
Range	10-80%
TMB (mut/Mb)	
Median	2.1 mut/Mb
Range	0-48.9 mut/Mb

Figure 2: Incidence of commonly mutated genes amongst the cohort and TCGA database

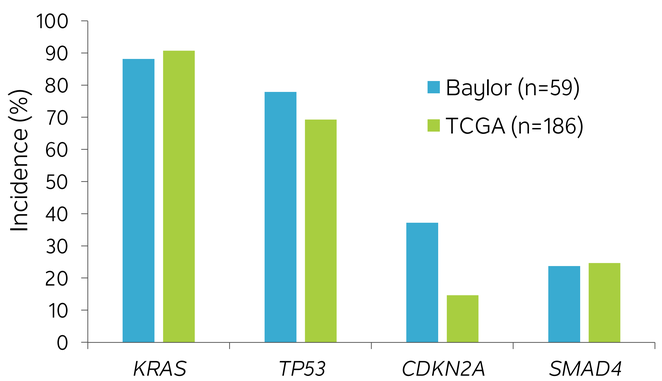

Figure 2. The most commonly mutated genes include *KRAS* (Baylor 88.1% vs. TCGA 90.7%) and *TP53* (Baylor 77.9% vs. TCGA 69.3%). *KRAS* VAF ranged from 1.7%-42.2%. *TP53* VAF ranged from 2.1%-57.4%. *CDKN2A* VAF ranged from 5.1%-36.2%, and 5/22 *CDKN2A* alterations were copy number losses. *SMAD4* VAF ranged from 4.1%-33.2%, and 4/14 *SMAD4* alterations were copy number losses.

Figure 3: Incidence of potentially actionable mutations or biomarkers

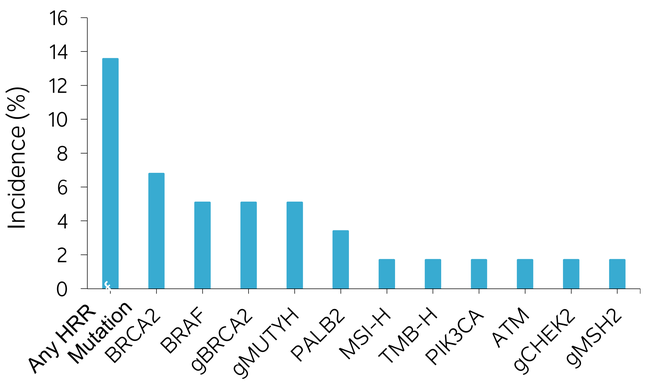

Figure 3. Overall incidence of any homologous recombination repair (HRR) mutations was 13.5%. Other notable mutations include *BRCA2 (6.8%)*, *BRAF (5.1%)*, *gBRCA2 (5.1%)* and *gMUTYH (5.1%)*. Targetable biomarkers include microsatellite instability high (MSI-H, 1.7%) and tumor mutational burden high (TMB-H, 1.7%). g indicates germline mutation.

CONCLUSIONS

- Comprehensive genomic profiling was performed on pancreatic FFPE tissues using Tempus|xT LDT at a clinical sequencing depth of 500x.
- Tempus|LENS reported *KRAS*, *TP53*, and *SMAD4* alteration detection rates comparable to the TCGA dataset.
- A subset of molecularly targetable mutations were detected via Tempus|xT, supporting the potential benefit of clinical genomic profiling.
- Overall, these results demonstrate the utility of combining genomic and clinical data, and support the routine use of FFPE tissue for clinical genomic profiling.

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