Real-World Characterization of PTK7, an Oncofetal Pseudokinase Expressed in Multiple Solid Tumors

Ursula A. Matulonis, MD[1]; Fernanda B. Musa, MD, MS[2]; Grace K. Dy, MD[3]; David J. Lennon, PhD[4]; David Dornan, PhD[4]; Ashwini B. Pai, PharmD[4]; Kathleen S. Keegan, PhD[4]; Kathleen N. Moore, MD[5]

[1]Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA; [2]Providence-Swedish Cancer Institute, Seattle, WA, USA; [3]Roswell Park Comprehensive Cancer Center, Buffalo, NY, USA; [4]Whitehawk Therapeutics, Morristown, NJ, USA; [5]Stephenson Oklahoma Cancer Center, Oklahoma City, OK, USA

Background

- Protein tyrosine kinase 7 (PTK7) is a pseudokinase shown to modulate the Wnt signaling pathway; it is involved in the regulation of cell polarity, migration, proliferation, and differentiation during embryogenesis[1,2]
- Although it is downregulated in normal adult tissue, studies have demonstrated aberrant overexpression of the PTK7 gene and protein in various tumor types, indicating PTK7 may be a valuable therapeutic target in oncology[1–4]
  - Immunohistochemical analyses of the PTK7 protein in normal and cancerous human tissue have shown consistent PTK7 overexpression in several tumor types, including, but not limited to, non-small cell lung cancer (NSCLC),[3,4] small cell lung cancer (SCLC),[3,4] and ovarian cancer[4]
- Previous studies using The Cancer Genome Atlas (TCGA) data have demonstrated consistent upregulation of *PTK7* expression in multiple solid tumor samples versus matched adjacent normal tissue[5,6]
  - However, TCGA studies may be limited by a smaller sample size relative to the Tempus AI real-world database (157,528 tumor samples) and overrepresentation of early-stage disease[7]
- The aim of this study was to characterize *PTK7* expression in a large patient population, spanning multiple tumor types at various disease stages

Methods

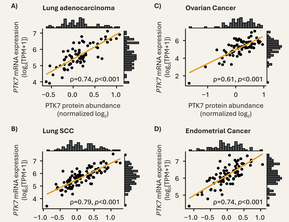
- PTK7 protein expression was analyzed using data from the Clinical Proteomic Tumor Analysis Consortium
  - Spearman correlation was used to assess the relationship between PTK7 protein abundance and *PTK7* mRNA expression
- Data from a real-world database (Tempus AI, Inc.) were analyzed for *PTK7* mRNA expression across multiple tumor types and across histologic subtypes and disease stages of lung, ovarian, and endometrial cancers. Gene expression data were derived from a whole-transcriptome RNA-sequencing panel (Tempus' xR) capturing 20,000 genes. DNA mutation status was informed by Tempus' solid tumor assay, xT, which captures 648 coding genes
  - The gene expression distributions of other targets of relevance in cancers overall and in lung, ovarian, and endometrial cancers were also analyzed
  - The weighted average pan-cancer median was calculated using incidence rates based on 2023 data for 17 solid cancers from the Surveillance, Epidemiology, and End Results (SEER) database—the indication-specific median expression value (Tempus' data) was multiplied by SEER incidence rates for each cancer, and the weighted average was calculated
- In NSCLC, expression of *PTK7* and other relevant targets was compared between epidermal growth factor receptor (*EGFR*) mutant and *EGFR* wild-type tumors in adenocarcinoma and squamous cell carcinoma (SCC) histologic subtypes
- Gene expression was quantified as $\log_2$(transcripts per million [TPM]+1), and group differences were analyzed using the Kruskal–Wallis or Mann–Whitney test

Results

PTK7 PROTEIN AND RNA EXPRESSION ARE WELL CORRELATED

- PTK7 protein abundance and *PTK7* mRNA expression were correlated across tumor types (lung adenocarcinoma, Spearman's rho [ρ]=0.74; lung SCC, ρ=0.79; ovarian cancer, ρ=0.61; endometrial cancer, ρ=0.74) (FIGURE 1)

FIGURE 1. Correlation Between PTK7 Protein Abundance and *PTK7* mRNA Expression in (A) Lung Adenocarcinoma, (B) Lung SCC, (C) Ovarian Cancer, and (D) Endometrial Cancer



ρ, Spearman's rho; **SCC**, squamous cell carcinoma; **TPM**, transcripts per million.

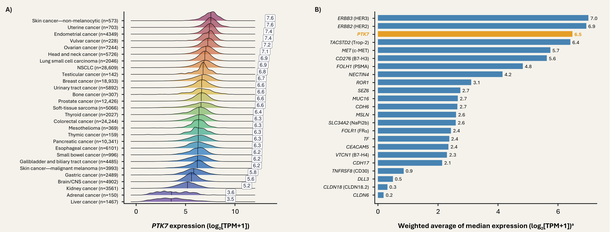
PTK7 IS HIGHLY EXPRESSED IN SOLID TUMORS

- *PTK7* mRNA expression was analyzed in 157,528 tumor samples, of which 75,756 (48.1%) were from metastatic tumors
- 70% of all solid tumor samples showed *PTK7* expression
- *PTK7* expression was observed across multiple tumor types, with most showing a normal distribution (FIGURE 2A)
  - Among groups with robust sample sizes (N ≥4000), tumor types with the highest median *PTK7* expression ($\log_2$[TPM+1]) were endometrial cancer (7.4), ovarian cancer (7.2), head and neck cancer (7.1), and NSCLC (6.9)
- Across tumor types, *PTK7* was one of the most highly expressed genes, alongside *ERBB2* (human epidermal growth factor receptor 2 [HER2]), *ERBB3* (HER3), and *TACSTD2* (Trop-2) (FIGURE 2B)
  - The numerical range of *PTK7* expression ($\log_2$[TPM+1]) was similar to that of *ERBB2* (HER2), across tumor types

PTK7 EXPRESSION IS HIGH ACROSS LUNG CANCER HISTOLOGIC SUBTYPES

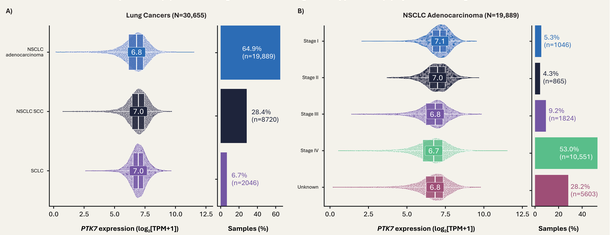
- *PTK7* expression was high across lung cancer histologic subtypes, with median $\log_2$(TPM+1) values of 6.8, 7.0, and 7.0 in NSCLC adenocarcinoma, NSCLC SCC, and SCLC, respectively (FIGURE 3A)
  - Within each histologic subtype, *PTK7* expression was stable across metastatic status and disease stage
- In NSCLC adenocarcinoma tumor samples, there was a modest decrease in median *PTK7* expression with advancing disease stage (stage 1, 7.1; stage 4, 6.7; $p<0.0001$ by Mann–Whitney test) (FIGURE 3B)
  - This expression was 6.7 and 7.0 in metastatic and primary tumor samples, respectively, and is not expected to be a biologically meaningful difference in expression

FIGURE 2. *PTK7* mRNA Expression (A) Across Tumor Types and (B) Relative to Other Therapeutic Targets



Gene expression data were derived from a whole-transcriptome RNA-sequencing panel (Tempus' xR) capturing 20,000 genes. *Across 17 indications (pan-cancer, N=122,228), weighted by SEER incidence. **CNS**, central nervous system; **NSCLC**, non-small cell lung cancer; **SEER**, Surveillance, Epidemiology, and End Results; **TPM**, transcripts per million.

FIGURE 3. *PTK7* mRNA Expression (A) Across Lung Cancer Histologic Subtypes and (B) by Disease Stage in NSCLC Adenocarcinoma



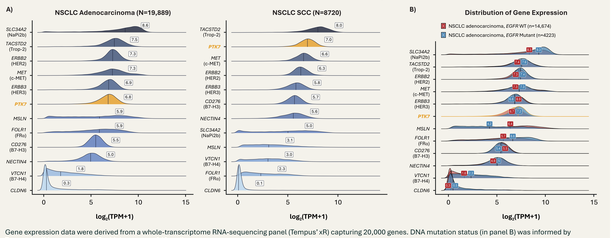
Gene expression data were derived from a whole-transcriptome RNA-sequencing panel (Tempus' xR) capturing 20,000 genes. **NSCLC**, non-small cell lung cancer; **SCC**, squamous cell carcinoma; **SCLC**, small cell lung cancer; **TPM**, transcripts per million.

- *PTK7* showed similar median expression to targets of antibody–drug conjugates (ADCs) approved or in late-stage development for the treatment of NSCLC, including *TACSTD2* (Trop-2), *ERBB2* (HER2), *MET* (c-MET), and *ERBB3* (HER3) (FIGURE 4A)
  - In NSCLC SCC, *PTK7* expression was higher than all key tumor markers, with the exception of *TACSTD2* (Trop-2) (FIGURE 4A)
- The prevalence of *EGFR* mutations was 22% in NSCLC adenocarcinoma samples compared with 5% in NSCLC SCC samples; this is consistent with previous analyses showing that more than 75% of NSCLC diagnoses in the United States are *EGFR* wild-type tumors[8]
- In NSCLC adenocarcinoma, *PTK7* expression was observed regardless of *EGFR* mutation status (FIGURE 4B)
  - Higher median expression ($\log_2$[TPM+1]) was observed in *EGFR* mutant versus *EGFR* wild-type tumors (7.2 vs 6.7; $p<0.0001$ by Mann–Whitney test), but this difference is not expected to be biologically meaningful

PTK7 EXPRESSION IS HIGH ACROSS ALL OVARIAN CANCER HISTOLOGIC SUBTYPES

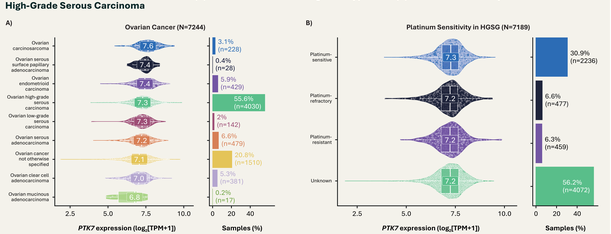
- *PTK7* was expressed across all ovarian cancer histologic subtypes, with median $\log_2$(TPM+1) values ranging from 6.8 in mucinous adenocarcinoma to 7.6 in carcinosarcoma (FIGURE 5A)
  - Within each histologic subtype, *PTK7* expression was generally stable across metastatic status and disease stage, with variations of <0.5 in median values
- *PTK7* expression was stable across disease stages in most subtypes of ovarian cancer, including high-grade serous carcinoma (HGSC): stage I (7.1), stage II (7.2), stage III (7.4), and stage IV (7.3)
  - In HGSC, median *PTK7* expression was stable across metastatic and primary tumors (7.3 in both)
- *PTK7* expression was similar in platinum-sensitive and platinum-resistant tumors (FIGURE 5B)

FIGURE 4. Distribution of Gene Expression in NSCLC Tumor Samples by (A) Histologic Subtype and (B) *EGFR* Mutation Status



Gene expression data were derived from a whole-transcriptome RNA-sequencing panel (Tempus' xR) capturing 20,000 genes. DNA mutation status (in panel B) was informed by Tempus' solid tumor assay, xT, which captures 648 coding genes.
EGFR, epidermal growth factor receptor; **NSCLC**, non-small cell lung cancer; **SCC**, squamous cell carcinoma; **TPM**, transcripts per million; **WT**, wild-type.

FIGURE 5. *PTK7* mRNA Expression Across (A) Ovarian Cancer Histologic Subtypes and (B) Platinum Sensitivity Status in High-Grade Serous Carcinoma



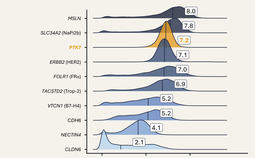
Gene expression data were derived from a whole-transcriptome RNA-sequencing panel (Tempus' xR) capturing 20,000 genes.
HGSC, high-grade serous carcinoma; **TPM**, transcripts per million.

- Across all ovarian cancer samples, median *PTK7* expression was high and showed a similar distribution to that observed for *ERBB2* (HER2) expression (FIGURE 6)
  - Median *PTK7* expression ($\log_2$[TPM+1]) was similar to that of *ERBB2* (HER2), *FOLR1* (FRα), and *TACSTD2* (Trop-2) (7.2, 7.1, 7.0, and 6.9, respectively), and showed a normal distribution compared with the wider distribution in expression observed with *FOLR1* (FRα) and *TACSTD2* (Trop-2)

PTK7 EXPRESSION IS HIGH ACROSS ENDOMETRIAL CANCER HISTOLOGIC SUBTYPES

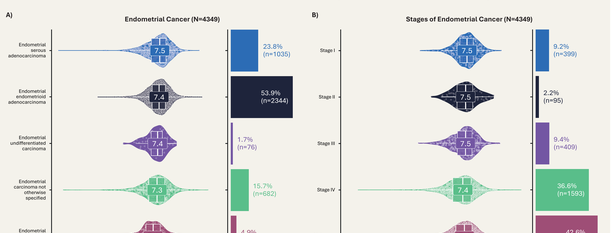
- *PTK7* expression was high across endometrial cancer histologic subtypes, with median $\log_2$(TPM+1) values of 7.1–7.5 (FIGURE 7A)
  - Within each histologic subtype, *PTK7* expression was stable across metastatic status and disease stage, with variations of <0.5 in median values
  - Expression was 7.4 and 7.5 in metastatic and primary tumor samples, respectively
- In endometrial cancer, *PTK7* expression remained consistent across disease stages (FIGURE 7B)

FIGURE 6. Gene Expression of Targets in Development for Ovarian Cancer in Ovarian Tumor Samples Across Histologic Subtypes (N=7244)



Gene expression data were derived from a whole-transcriptome RNA-sequencing panel (Tempus' xR) capturing 20,000 genes. **TPM**, transcripts per million.

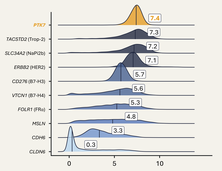
FIGURE 7. *PTK7* mRNA Expression Across (A) Endometrial Cancer Histologic Subtypes and (B) Disease Stages



Gene expression data were derived from a whole-transcriptome RNA-sequencing panel (Tempus' xR) capturing 20,000 genes. **TPM**, transcripts per million.

- In endometrial cancer tumor samples, median expression of *PTK7* was 1.2- to 128-fold higher than that of all other biomarkers tested, including *TACSTD2* (Trop-2) and *ERBB2* (HER2) (FIGURE 8)
  - *PTK7* expression showed a normal distribution that was similar to the distribution for *ERBB2* (HER2) expression

FIGURE 8. Distribution of Gene Expression in Endometrial Tumor Samples Across Histologic Subtypes (N=4349)



Gene expression data were derived from a whole-transcriptome RNA-sequencing panel (Tempus' xR) capturing 20,000 genes. **TPM**, transcripts per million.

Conclusions

- *PTK7* shows differential expression in tumor versus normal tissue, with strong correlations between *PTK7* mRNA and PTK7 protein abundance
- These data suggest that, on average, *PTK7* is one of the most highly expressed targets across solid tumors
- Lung, ovarian, and endometrial cancers show robust *PTK7* expression across histologic subtypes
  - In NSCLC, *PTK7* expression is observed regardless of *EGFR* mutation status
- *PTK7* is expressed at levels comparable to several validated ADC targets, underscoring its clinical potential
  - These include *ERBB3* (HER3) and *MET* (c-MET) in lung cancer, *FOLR1* (FRα) in ovarian cancer, and *TACSTD2* (Trop-2) and *ERBB2* (HER2) in lung, ovarian, and endometrial cancers
- *PTK7* expression remains high across disease stages, supporting its relevance in early- and late-stage disease
- These data suggest cross-indication applicability of targeting PTK7, and thereby support its potential as a pan-tumor ADC target that warrants further investigation

REFERENCES

1. Mottard K, et al. *Oncologist*. 2025;30:oyae290.
2. Dessaux C, et al. *Oncogene*. 2024;43:1973–84.
3. Kong C, et al. *Mol Cancer Ther*. 2023;22:1128–43.
4. Damelin M, et al. *Sci Transl Med*. 2017;9:eaag2611.
5. Raivola J, et al. *Cell Death Dis*. 2022;13:714.
6. Kim MH, et al. *Cells*. 2025;14:181.
7. Jin Z, et al. *Front Oncol*. 2024;14:1448695.
8. Zhang Y-L, et al. *Oncotarget*. 2016;7:78985–93.

ACKNOWLEDGMENTS and DISCLOSURES

This study was sponsored by Whitehawk Therapeutics, Morristown, NJ, USA. Data generation and data analysis were provided by Lennart Langouche and Daiyana Delgado of Tempus AI, Chicago, IL, USA. Medical writing support was provided by Farhana Burnett, PhD, CMPP, and Holly Strausbaugh, PhD, of Twist Medical, and funded by Whitehawk Therapeutics.

Corresponding author: Grace K. Dy, MD (Grace.Dy@RoswellPark.org)

Grace K. Dy reports consulting fees from Whitehawk Therapeutics. For disclosures of co-authors, please refer to the abstract.

Presented at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics; Boston, MA, USA; October 22–26, 2025