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Gene Signature Panel for Predicting Response to Immune Checkpoint Blockade in Solid Tumors

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Background & Unmet Need	Technology Overview	Inventors: Timothy McGraw Nasser Altorki Patents: US Application Filed Publications: Altorki et al. Cell Rep Med. 2024. Biz Dev Contact: Brian Kelly (646) 825-2766 bjk44@cornell.edu Cornell Reference: D-10833
- While immune checkpoint blockade (ICB) therapies have transformed the management of solid tumors, only a small subset of patients achieve durable response (~20%) - PD-L1 expression is the most validated biomarker for predicting response to ICB, but shows inconsistency across treatment settings and may miss responders with low PD-L1 scores - Moreover, issues with detection and heterogeneity within and between tumor types further confounds the predictive value of PD-L1 - Other known biomarkers, such as tumor mutational burden (TMB), encounter challenges with standardizing cut-off values and demonstrating predictive accuracy across different tumor types, especially in those without ICB approval Unmet Need: Molecular signatures to identify patients likely to respond to ICB therapies across a variety of solid tumors	The Technology: A 140-gene signature identifying a molecular subclass likely to respond to immune checkpoint blockade across various solid tumors The Discovery: RNA-seq data from a phase II trial of stereotactic body radiation therapy (SBRT) combined with anti-PD-L1 (durvalumab) in NSCLC revealed genes linked to highly proliferating cells - This subclass is dominated by increased expression of cell cycle genes, as well as increased glycolysis, TMB, and immune suppression PoC Data: The 140-gene set was associated with reduced DFS and OS in lung adenocarcinoma with a hazard ratio of 1.6 ($p = 3.04 \times 10^{-6}$) 140-gene set was also tested against an additional five TCGA solid tumor types and demonstrated correlation with survival in breast, prostate, melanoma, and pancreatic cancer - This molecular subclass is present in one-quarter to two-thirds of tumors, varying by disease	



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DFS: Disease-free Survival ; **ICB:** Immune Checkpoint Blockade ; **NSCLC:** Non-small cell lung cancer
OS: Overall Survival ; **SBRT:** Stereotactic Body Radiation Therapy ; **TMB:** Tumor Mutational Burden
TCGA: The Cancer Genome Atlas

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Technology Applications

- Identification of patients likely to respond to ICB or ICB in combination with SBRT in lung adenocarcinoma, melanoma, breast cancer, prostate cancer and pancreatic cancer
- ICB may include anti-PD/PD-L1 and anti-CTLA-4 therapies

Technology Advantages

- Broad applicability across multiple solid tumor types beyond lung cancer
- The 140-gene signature reflects biology independent of EGFR mutation status, TMB, and PD-L1/P1 expression

Supporting Data / Figures

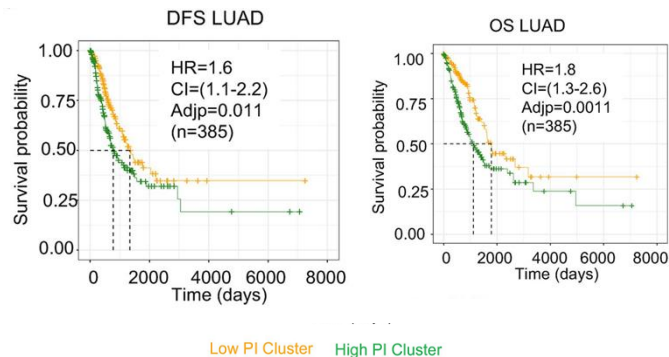


Figure 1: High proliferation index (PI) tumors (140-gene set) were associated with reduced disease-free and overall survival in lung adenocarcinoma samples from The Cancer Genome Atlas (TCGA).

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[US Application Filed](#)

Publications:

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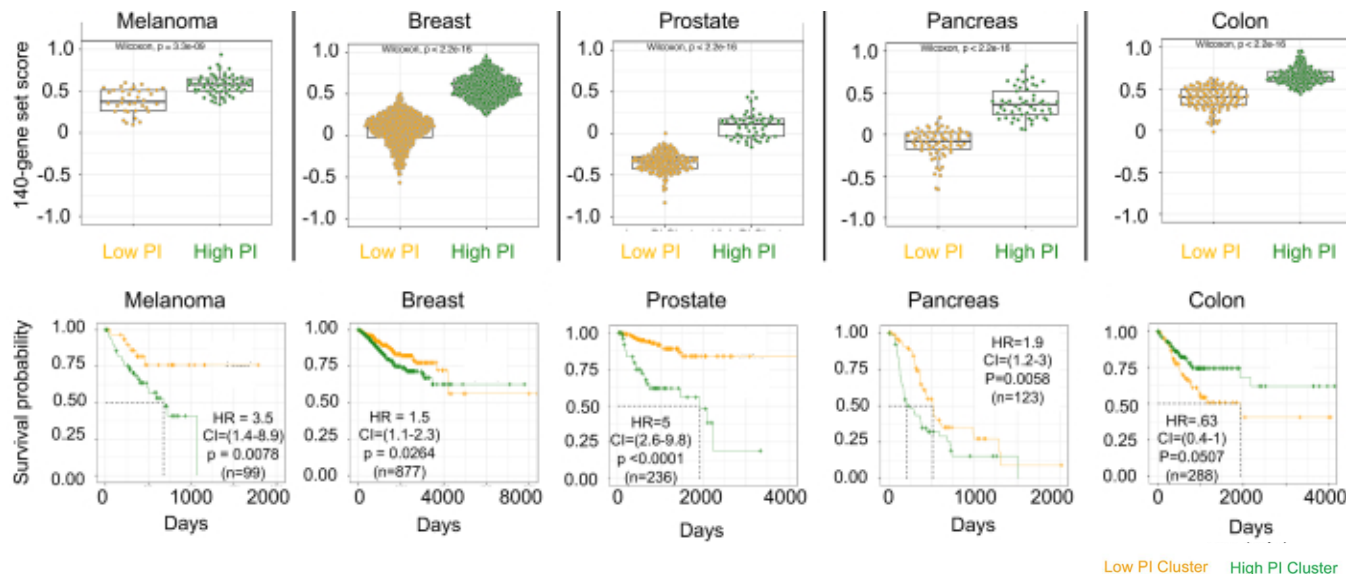


Figure 2: The 140-gene signature was used to cluster TCGA RNA-seq data of five different solid tumor types. All five tumor types were robustly clustered into two groups. High PI tumors (140-gene set) were associated with reduced survival in all melanoma, breast, prostate, and pancreatic cancers but not in colon cancer.

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