



Weill Cornell Medicine

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

Lead Inventors:

Timothy McGraw, Ph.D.

Professor of Biochemistry in Cardiothoracic Surgery,
Cardiothoracic Surgery , Weill Cornell Medical College

Professor of Biochemistry, Biochemistry , Weill Cornell
Medical College

Nasser Altorki, M.D.

David B. Skinner, M.D. Professor of Thoracic Surgery,
Cardiothoracic Surgery , Weill Cornell Medical College

Professor of Cardiothoracic Surgery, Cardiothoracic
Surgery , Weill Cornell Medical College

Business Development Contact:

Brian Kelly

Director, Technology Licensing

(646) 962-7041

bjk44@cornell.edu

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Background & Unmet Need	Technology Overview	Inventors: Timothy McGraw Nasser Altorki Patents: PCT Application Filed Publications: Altorki et al. Cell Rep Med. 2024. Biz Dev Contact: Brian Kelly 646-962-7041 bjk44@cornell.edu Cornell Reference: D-10833
<ul style="list-style-type: none"> 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 	<ul style="list-style-type: none"> 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 	

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

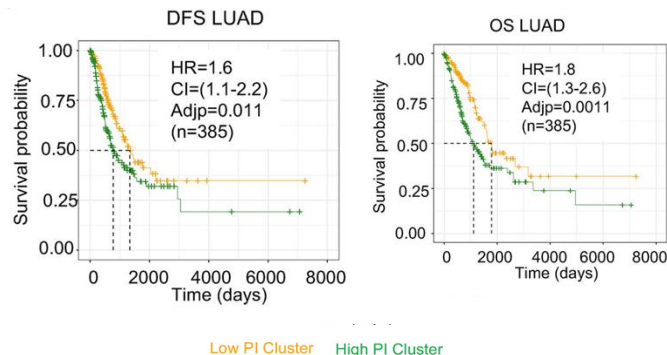


Figure 1: High proliferation index (PI) tumors (140-gene set) were associated with increased disease-free and overall survival in lung adenoma adenoma samples from The Cancer Genome Atlas (TCGA).

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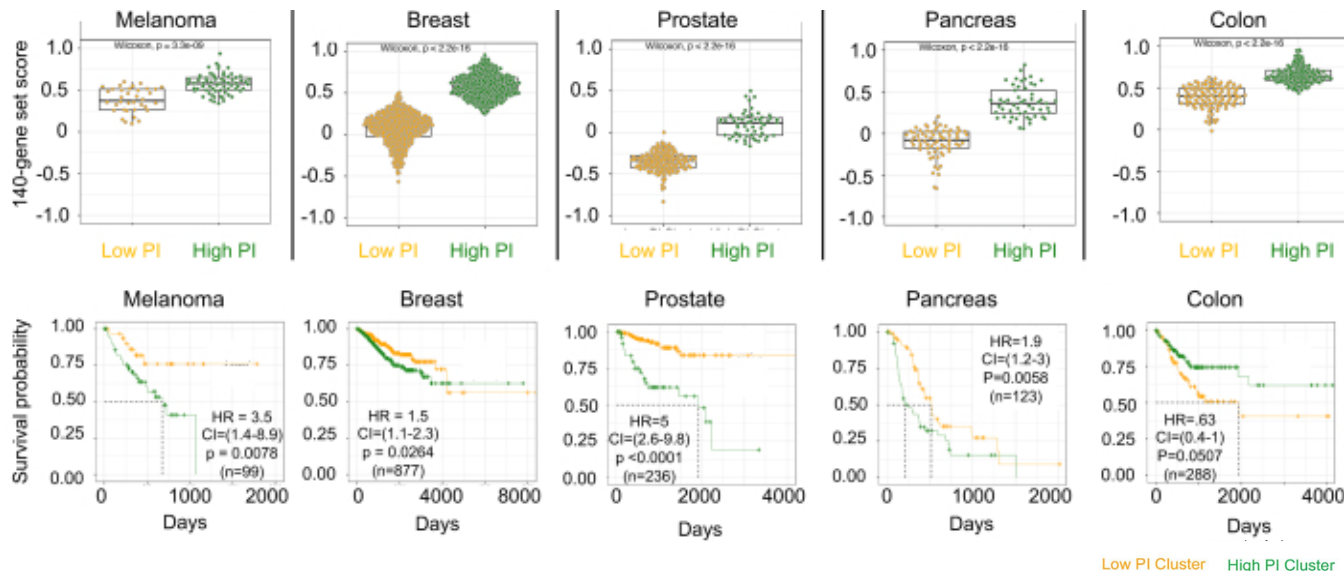


Figure 2: The 140-gene signature was used to cluster TCGA RNA-seq data of five different solid tumor types. All five tumor types were robustly clustered into two groups. High PI tumors (140-gene set) were associated with increased survival in all melanoma, breast, prostate, and pancreatic cancer but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

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