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

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

Background & Unmet Need

- 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

Technology Overview

- **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

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

Weill Cornell Medicine

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

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

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

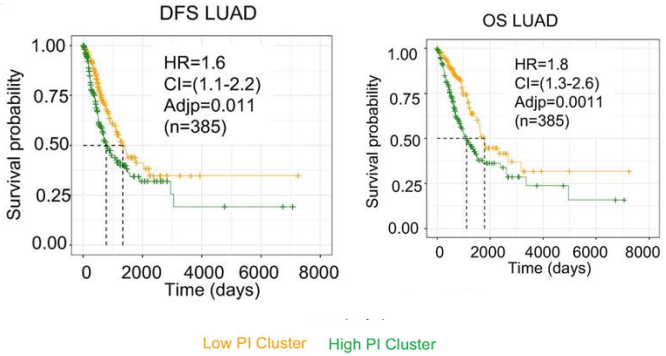

Figure 1: High proliferation index (PI) tumors (140-gene set) were associated with increased disease-free and overall survival in lung adenoma adenoma samples from The Cancer Genome Atlas (TCGA).

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

Weill Cornell Medicine

DFS: Disease-free Survival ; **ICB:** Immune Checkpoint Blockade; **OS:** Overall Survival
SBRT: Stereotactic Body Radiation Therapy ; **TMB:** Tumor Mutational Burden

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

Supporting Data / Figures

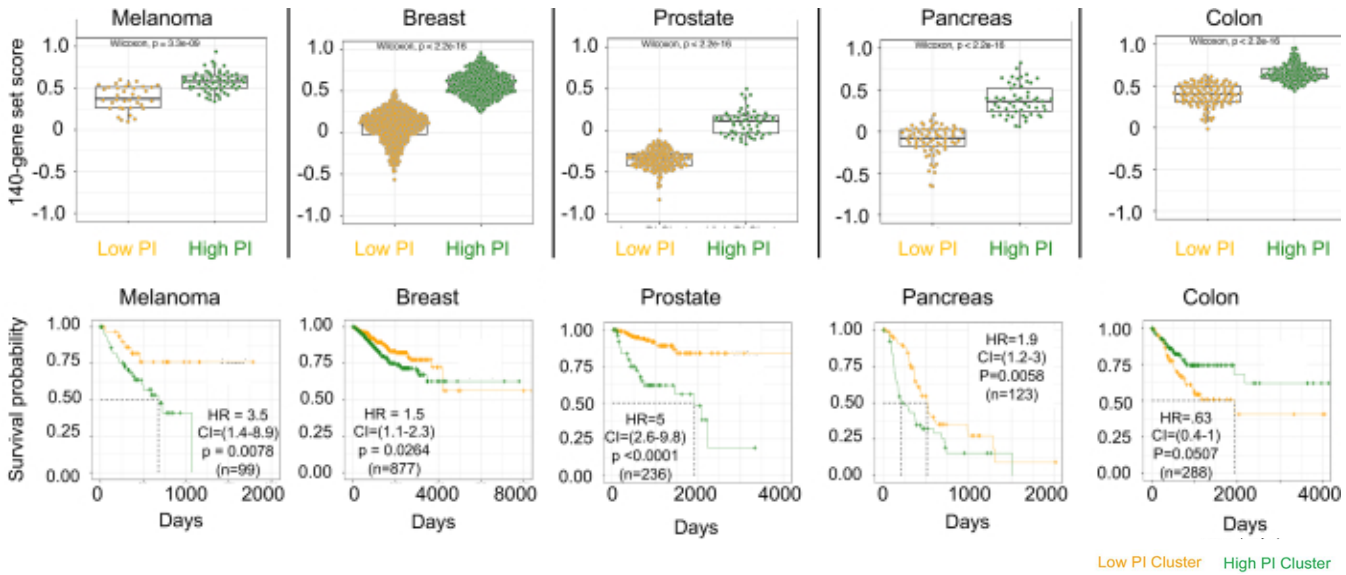

Figure 2: The 140-gene signature was used to cluster TCGA RNA-seq data of five different solid tumor types. All five tumor types were robustly clustered into two groups. High PI tumors (140-gene set) were associated with increased survival in all melanoma, breast, prostate, and pancreatic cancer but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

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

Weill Cornell Medicine

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

Weill Cornell Medicine