Machine learning-based immune phenotypes correlate with STK11/KEAP1 co-mutations and prognosis in resectable NSCLC: a sub-study of the TNM-I trial

Background

Non-small cell lung cancer (NSCLC) is a heterogeneous disease, and patient responses to treatment vary significantly even within the same clinical stage. Tumor-immune interactions are crucial in determining prognosis and treatment response. This study used machine learning (ML) to classify immune phenotypes in several cohorts of NSCLC patients and determined their association with genomic alterations and differential gene expression patterns. By analyzing the spatial distribution of CD8+ T-cells, the study aimed to develop a predictive model that can identify patients at higher risk of disease recurrence following surgical resection.

Research Questions

- Can machine learning-based immune phenotyping help predict prognosis in resectable NSCLC?
- What is the relationship between ML-derived immune phenotypes and established nCounter immune signatures?
- Can immune phenotyping improve the prediction of disease recurrence after surgery in early-stage NSCLC?

Results & Conclusions

- The ML-based immune phenotyping model classified tumors into three categories: inflamed, altered, and desert.
- The inflamed phenotype associated with better prognosis and longer disease-specific survival (DSS) and time to recurrence (TTR).
- The inflamed phenotype was a significant independent predictor of prolonged DSS and TTR in the retrospective cohort.
- STK11 and KEAP1 mutations were more frequently found in non-inflamed tumors and were linked to poor immune cell infiltration.
- Due to its robustness and reliability, the nCounter platform was used to validate the ML-determined immune signatures.
- nCounter orthogonal validation demonstrated that the inflamed phenotype correlated with upregulated adaptive immunity gene signatures, including increased CD8+ T-cell density.
- Validating with nCounter built confidence in the new ML-based method for clinical sample screening.

Experimental Setup

Sample Type	NSCLC tumor samples from stage I-IIIA resected patients
Tissue Type	Whole tissue sections
Assay	nCounter® PanCancer IO 360™ Panel
Analyte	RNA
Instrument	nCounter® Analysis System

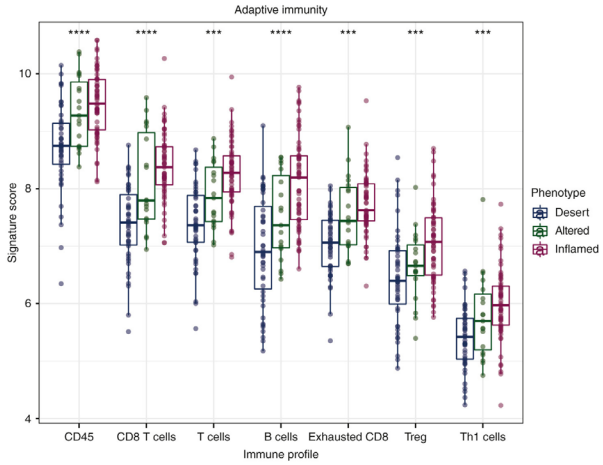

Figure 2: Immune Signatures. Immune cell scores from the nCounter IO 360 panel, organized by the ML-driven immune subclass (desert, altered, or inflamed).

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