Transcriptomic AI-based classification of immune phenotypes for predicting immunotherapy response in lung cancer

Ki Wook Lee[1], Hyun Woo Park[1], Sehhoon Park[2], Balachandran Manavalan[1] and Young-jun Jeon[1]
[1]Sungkyunkwan University, Suwon, Gyeonggi-do, Republic of Korea
[2]Samsung Medical Center, Seoul, Republic of Korea

I. SUMMARY

Despite the success of immune checkpoint inhibitors (ICIs) in treating advanced non-small-cell lung cancer (NSCLC), robust biomarkers for predicting therapeutic response remain limited. While tumor-infiltrating lymphocytes (TILs) have shown promise, conventional assessment using H&E-stained slides is labor-intensive, subjective, and spatially constrained.

To overcome these limitations, we developed an AI-driven immune phenotyping model using transcriptomic profiles from 449 TCGA-LUAD samples annotated by Lunit-SCOPE[1]. Rather than relying on conventional gene selection, we identified AI-based important genes (AIGs) using six tree-based machine learning (ML) algorithms applied to the entire genes. These AIGs were used to train immune infiltration models across 15 machine learning and deep learning (DL) algorithms, further enhanced via ensemble strategies.

Our study highlights the potential of AI-driven transcriptomic analysis to inform immunotherapy decisions in clinical settings

II. Main

A. Methods

We analyzed transcriptomic data from 449 lung adenocarcinoma (LUAD) samples obtained from TCGA, each annotated with immune phenotypes via Lunit SCOPE. Samples were randomly divided into training (80%) and test (20%) sets.

Without prior gene filtering, AI-informed genes (AIGs) were identified using six tree-based machine learning algorithms applied to the full gene expression profiles. Final classification models were constructed using 15 ML/DL algorithms, incorporating ensemble learning.

Model performance was further validated on an external cohort of 76 LUAD samples from Samsung Medical Center (SMC).

B. Results

Our model achieved an AUC of 1.0 in the training cohort and 0.86 in the SMC validation cohort for immune phenotype classification. When applied to ICI response prediction, the model reached an AUC of 0.769.

Notably, two novel biomarker candidates were identified from the AIG set, demonstrating potential utility for guiding immunotherapy in NSCLC.

C. Discussion

This novel framework holds strong potential for future applications in cell-free transcriptomics, particularly in settings where transcriptomic signatures are extremely diluted.

III. ILLUSTRATIONS

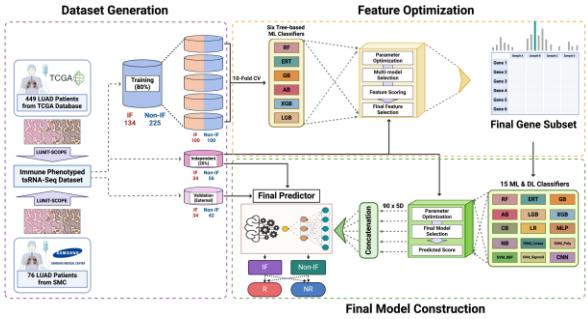

Figure 1: Overall framework of AI-based Immune phenotyping model using transcriptomics

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