

Immune and Transcriptomic Signatures Predict Prognosis in Neoadjuvant Immunotherapy of Lung Cancer

Yixin Liu, Fangjun Chen, Shu Su, Xin Lv, Lianjie Li, Mengging Wang, Lifeng Wang

Nanjing Drum Tower Hospital, the Affiliated Hospital of Nanjing University Medical School, Nanjing, China



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OBJECTIVE: To identify transcriptomic and immune signatures associated with pathologic complete response (pCR) and prognosis in patients with resectable non-small cell lung cancer (NSCLC) treated with neoadjuvant immunotherapy plus chemotherapy.

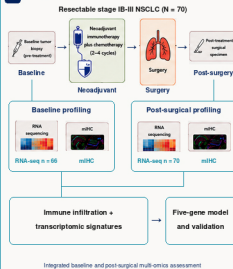
BACKGROUND

Neoadjuvant immunotherapy plus chemotherapy has improved outcomes in resectable NSCLC, but biomarkers predicting pathologic complete response (pCR) and prognosis remain limited. This study investigated transcriptomic and immune features associated with treatment response.

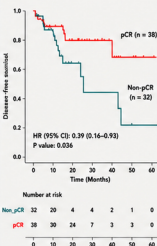
METHODS

- Study design:** Retrospective cohort study.
- Patients:** 70 patients with stage IB-III resectable NSCLC treated at Nanjing Drum Tower Hospital between 2022 and 2025.
- Treatment:** Neoadjuvant immunotherapy plus chemotherapy followed by surgery.
- Samples:** Baseline tumor biopsies (pre-treatment) and post-treatment surgical specimens.
- Assays:** RNA sequencing (RNA-seq) and multiplex immunohistochemistry (mIHC).
- RNA-seq:** baseline n = 66; post-surgical n = 70.
- Analyses:** Immune cell infiltration, transcriptomic signatures, dynamic changes (pre vs. post) and five-gene model evaluation.
- Model:** A five-gene predictive model for pCR and prognosis was developed and validated.

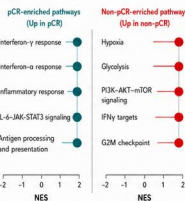
1 Study design and workflow



2 Disease-free survival by response (n = 70)

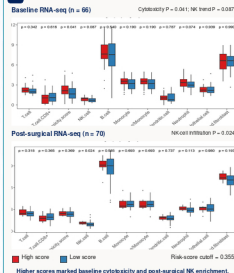


3 Pathway enrichment by response



Gene set enrichment analysis of baseline tumors shows immune and interferon pathways enriched in pCR, whereas metabolic, proliferative, and cell cycle pathways are enriched in non-pCR.

4 Five-gene model: Immune contexture



KEY FINDINGS

- Five-gene model AUC = 0.866
- pCR predicts superior DFS
- NK-cell activation is a hallmark of response
- CMK2 is strongly linked to immune activation



KEY CLINICAL IMPLICATIONS

- The five-gene model may aid in predicting pCR and selecting patients who benefit from neoadjuvant immunotherapy.
- Monitoring NK-cell activation and CMK2-associated chemokine signatures could inform treatment response.
- These biomarkers may guide future trials and personalize perioperative immunotherapy strategies.

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Authors: Yixin Liu, Fangjun Chen, Shu Su, Xin Lv, Lianjie Li, Mengging Wang, Lifeng Wang

Institution: Nanjing Drum Tower Hospital, the Affiliated Hospital of Nanjing University Medical School, Nanjing, China

DISCLOSURE:
The authors declare no conflict of interest.

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Corresponding to: Lifeng WANG
Email: lifengwang@njmu.edu.cn

