

Explainable Computational Methods for Predicting Treatment Response to Immunotherapy from Histology Images of Non-Small-Cell Lung Cancer

Non-small-cell lung cancer (NSCLC) accounts for approximately 85% of all lung cancer cases, making it the leading cause of cancer-related deaths globally. Post-surgical recurrence and treatment resistance are the main causes of cancer-related mortality. In the past decade, immune checkpoint inhibitors have revolutionized the therapeutic landscape for NSCLC. In patients lacking targetable oncogenic driver mutations, anti-PD-1/PD-L1 antibodies have become the backbone of first-line therapy. Although several anti-PD-1/PD-L1 antibodies have demonstrated clinical benefit in NSCLC treatment, the objective response rate ranges from 27% to 45%, indicating that the treatment benefit is limited to only a subset of patients. Developing reliable approaches for predicting treatment response is essential for guiding the selection of therapeutic strategies.

Inventors at Stanford have developed a computational method, called NucSegAI, that predicts the likelihood of a patient responding to immune checkpoint inhibitor-based immunotherapy using H&E- stained histology images of tumor tissues. The method takes histology images as input and follows a four- step workflow.

1. **Cell Nuclei Segmentation and Classification:** The method first segments cell nuclei from histology images and classifies them into five different types using a deep-learning model we developed.
2. **Spatial Relationship Modeling:** It then models the spatial relationships between different cell types using a graph-based computational algorithm.

3. **Lymphocyte Classification:** Lymphocytes are classified into ten distinct categories based on their morphological, textural and topological features.
4. **Treatment Response Likelihood Calculation:** Finally, the method calculates the likelihood of treatment response based on the proportions of lymphocytes in each category.

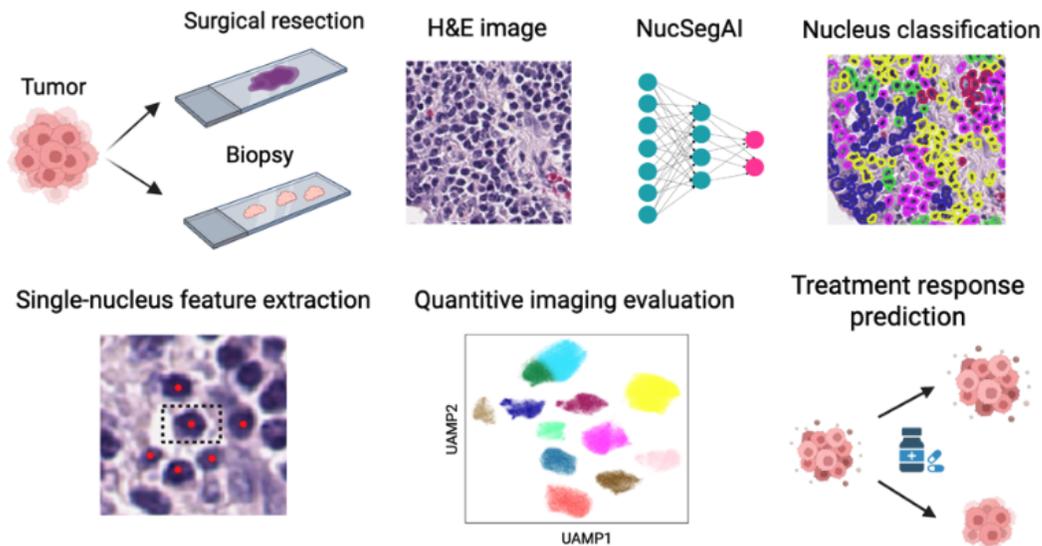


Image provided by the inventors

The described method has the potential to be commercialized as a tool for decision support, a service for personalized medicine, and a research tool, which will benefit biotechnology companies, pharmaceutical companies and academic researchers.

Stage of Development

Prototype

Advantages

The primary competitors of NucSegAI are PD-L1 immunohistochemistry (IHC) assays, which are currently the standard companion diagnostics used to guide immunotherapy decisions in non-small cell lung cancer. Compared to these assays, NucSegAI offers several key advantages in terms of tissue requirements, predictive accuracy, cost-effectiveness and scalability, turnaround time, and interpretability (see **Table 1** below).

1. **Input Requirements:** Unlike conventional PD-L1 assays that consume valuable tissue sections and require additional staining with proprietary antibodies, NucSegAI requires routine H&E-stained slides, which are already standard in diagnostic workflows.
2. **Predictive Accuracy:** NucSegAI demonstrates higher predictive performance compared to PD-L1 IHC assays.
3. **Cost and Scalability:** Traditional IHC assays require specialized platforms and licensed reagents, which increase cost and limit scalability. In contrast, NucSegAI can be deployed on standard digital pathology infrastructure using only H&E images, enabling large-scale, cost-efficient analysis.
4. **Interpretability:** Whereas PD-L1 assays provide binary or semiquantitative scores, NucSegAI outputs quantitative, spatially resolved maps of cell types and interactions.
5. **Automation:** PD-L1 assessment typically requires manual interpretation by pathologists and is subject to inter-observer variability. NucSegAI, once trained, provides a fully automated and reproducible pipeline.

Table 1. Comparison of NucSegAI with existing products

Metric	NucSegAI	Competitors
Sensitivity	High*	Moderate
Specificity	High*	Moderate-High
Cost	Very low	Moderate
Time-to-diagnosis	Minutes to hours	days
Ease-of-use	Easy	Moderate
Interpretability	Quantitative	Binary or semiquantitative
Technology integration	Easy	Moderate
<i>*To be validated in prospective studies</i>		

Applications

- Clinical trial optimization
- Personalized medicine tool

- Digital pathology tool
- Immunotherapy research tool

Publications

- Zheng, Y., Sadée, C., Ozawa, M., Howitt, B. E., & Gevaert, O. (2025). "[Single-cell multimodal analysis reveals tumor microenvironment predictive of treatment response in non-small cell lung cancer.](#)" Science Advances, 11(21), eadu2151.

Innovators

- Yuanning Zheng
- Olivier Gevaert

Licensing Contact

Sam Rubin

Licensing Associate, Life Science

[Email](#)