Our deep learning framework predicts immunotherapy treatment response on pre-treatment NSCLC biopsies with an AUC of 0.7.

Deep learning-based quantification of immune infiltrate for predicting response to pembrolizumab from pre-treatment biopsies of metastatic non-small cell lung cancer: A study on the PEMBRO-RT Phase 2 trial

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Introduction

Current clinical practice uses the PD-L1 expression-based Tumor Proportion Score (TPS) to stratify patients for immunotherapy treatment. Tumors with high TPS are more resistant to T-cell induced cell death, but can be treated with Immune Checkpoint Inhibitors (ICI), such as Pembrolizumab. However, TPS still insufficiently stratifies patients that do/do not respond to ICI.

We hypothesize that the Tumor Infiltrating Lymphocyte (TIL) densities within/surrounding the tumor will complement this stratification. In this study, we used a Deep Learning (DL) framework to examine the immune infiltrate (INF), a proxy for TILs, as a predictive and prognostic biomarker.

Goals:
- Predict pembrolizumab response using TIL features
- Extract TIL features using Artificial Intelligence (AI)
- Use H&E slides from pre-treatment mNSCLC biopsies

Methods

Analysis was carried out on a set of 61 H&E slides from pre-treatment biopsies. The HoVerNet deep learning network was used to segment and classify all cells on the slides. Tumor cells were postprocessed into tumor tissue masks. The tumor-associated stroma was approximated as tissue within a 100um / 500um radius from the tumor mask. The immune cells were counted within the defined tissue regions, and INF density features were calculated.

The INF features’ were analysed using ROC analysis and Kaplan Meier (KM) analysis to evaluate their predictive and prognostic value respectively. Stable disease at 12 weeks was used as endpoint for response, whereas progression free survival in months was used as endpoint for prognosis.

Results

All evaluated INF features were numerically greater in responders. All evaluated INF features some predictive value with AUCs > 0.63, where tumor-INF reported an AUC of 0.70.

KM analysis showed p=0.08 if patients were stratified based on the median tumorINF, and p=0.02 if stratified based on the optimal operating point of its ROC curve on treatment response.

Conclusion

DL models that analyze the immune infiltrate density on H&E whole slide images can identify mNSCLC responders to pembrolizumab.

Future work

- Improve tissue segmentation model
- Combine INF features with PD-L1 features
- Use DL to learn how to interpret the tumor tissue, tumor-associated stroma, and immune cells masks. Instead of aggregating them into feature values.

No conflicts to declare