Evaluating the Predictive Power of spaTIL and denTIL Features in Non-Small Cell Lung Cancer Response to Immunotherapy

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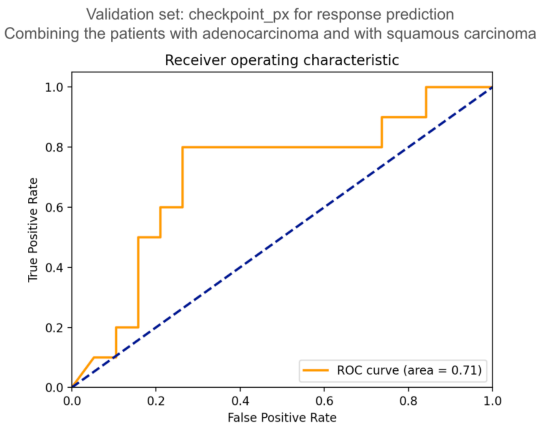
Abstract:

Background: The density of tumor-infiltrating lymphocytes (denTIL) and their spatial interplay with tumor cells (spaTIL) within the tumor microenvironment have emerged as significant indicators of immunotherapy (IO) response in non-small cell lung cancer (NSCLC). This study aimed to develop a model based on computationally measured spaTIL and denTIL on digital pathology slides to predict IO response for NSCLC.

Methods: NSCLC patients treated with IO from three institutes : Yale University (yale_io, N=74), Cleveland Clinic (ccf_io, N=51), and Northwestern University (nw_io, N=40) were collected in this study. Only patients with adenocarcinoma or squamous cell carcinoma were included in analysis. First, spaTIL and denTIL features were extracted from digital pathology slides of the patients included. Then, a multilayer perceptron based model trained with the spaTIL and denTIL features was developed on the training set (yale_io + ccf_io, N = 77) to stratify patients into either the response group (complete response or partial response) and non-response group (stable disease and progressive disease). The model was validated on an external validation set (nw_io, N=29).

Results: 25% patients in the training set responded to IO and 34% patients in the validation set responded to IO. The optimal hyper-parameters were locked down based on the AUC in 3-fold cross validation on the train set. The model with the selected optimal hyper-parameters generated AUC of 0.71 on the external validation set.



Conclusion: We demonstrated the TIL based signature is able to predict response to immunotherapy for NSCLC. The findings underscore the potential of these features in guiding treatment decisions, though further validation in larger, diverse cohorts is necessary to refine their predictive accuracy and clinical applicability.

This early experiment already outperformed the current biomarker standard in the space, PD-L1, which showed to have an AUC of 0.64 in the same validation dataset.