#1320P

I3LUNG: Digital pathology predicts PD-L1 expression in metastatic NSCLC patients treated with immunotherapy

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I3LUNG

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I3LUNG

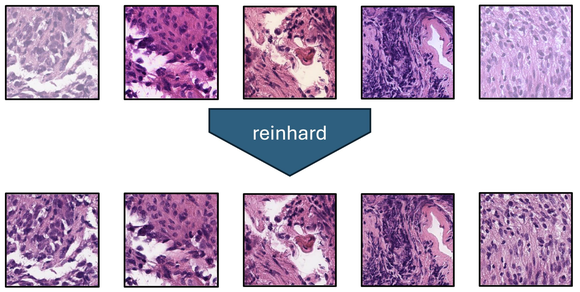
I3LUNG is a project funded by the European Union through the Horizon 2020 program that aims to develop Artificial Intelligence (AI)-based tools to predict the response of advanced non-small cell lung cancer (NSCLC) patients to immune checkpoint inhibitors (ICIs). The project brings together a consortium of 16 partners from 10 countries (Belgium, Denmark, Italy, Germany, Greece, Spain, Sweden, Switzerland, the United States, and Israel). Utilizing patient data, which includes digital pathology slides (DPS), genomics, radiomics, along with other patient characteristics, the overall goal is to develop a platform to guide therapeutic decisions in immuno-oncology for both healthcare professionals and patients.

INTRODUCTION

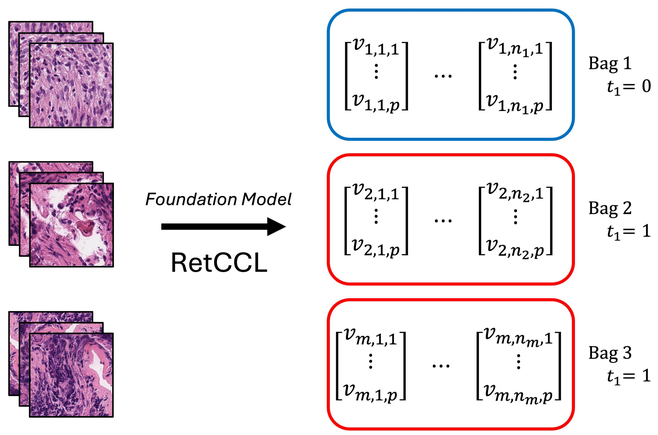
- Immunotherapy (IO) is the new standard of care for patients with advanced NSCLC, yet only 30-50% of patients benefit from it long-term.
- A better understanding of tumor features could help guide treatment decisions.
- To date, Programmed Death-Ligand 1 (PD-L1) remains the only biomarker used to predict IO efficacy, demonstrating its unique predictive ability, even if not perfect.
- A specific morphology has been found to be associated with PD-L1 expression, introducing new scenarios for the biological interpretation of the immune response.
- Utilizing AI and machine learning processes to analyze DPS could help create decision making tools for more individualized prediction of response.

METHODS

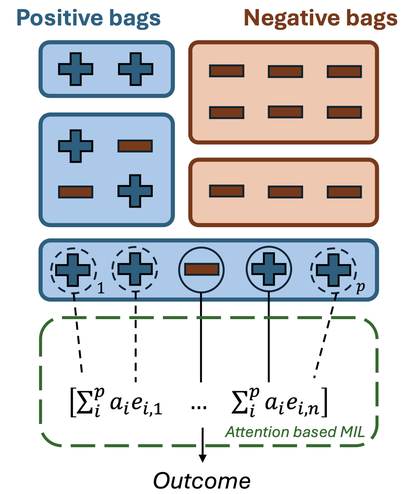
Digital Pathology whole slide images are very large images, and to feed them into Artificial Neural Network-based models we extracted square tiles [299x299px] at 10x magnification from the whole slide images.



Reinhard normalization was employed to reduce batch effect.



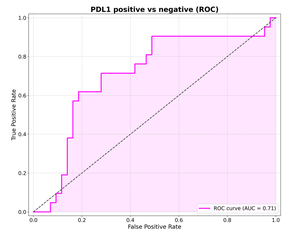
Large-scale AI models, known as foundation models, are developed using vast datasets and a training approach called self-supervised learning. This method does not rely on manually labeled data. Instead, it presents the model with a complex task inherent to the data itself. By solving this task, the model learns to identify and extract important features from the input information on its own.
For this task, we used RetCCL, a model trained on TCGA and PAIP datasets.
Once processed through RetCCL, tiles are converted into vectors of biologically relevant features.

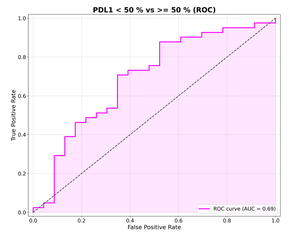


Slides are now converted into bags of vectors.
Assuming that not all tiles are equally relevant for our task, we need a model able to learn not only the patterns associated with a certain outcome, but also which tiles to focus on to find those patterns.
For this goal, we used an Attention-Based Multiple Instance Learning model, which employs the attention mechanism to infer the importance of each tile vector.

RESULTS

- Among the 2188 pt enrolled in the I3LUNG retrospective cohort, 474 patients had available DPS and PD-L1 status to be considered for the present analysis.
- PD-L1 expression was high (>50%), low (1-49%) and negative in 145 (37%), 129 (32%) and 127 (31%) patients within the training cohort, respectively, and 24 (33%), 23 (32%) and 26 (35%) among the validation cohort, respectively.
- PD-L1 high vs low/negative status through DPS were able to be predicted with an area under the curve (AUC) of 0.69; while for PD-L1 positive vs negative an AUC of 0.71 was achieved.





CONCLUSIONS

- To our knowledge, this is the largest series to date demonstrating a correlation between morphological features and PD-L1 expression in lung cancer.
- Data suggests that PD-L1 high and negative have different morphological phenotype.
- This rapid and generalizable model underscores the potential for morphological features to serve as valuable biomarkers in elucidating the mechanisms of immune responses.
- Within I3LUNG integration of genomic and radiomic data will probably allow to improve the ability to assess patient prognosis at diagnosis.

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Scan here to view a plain language summary of this study.

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