Single cell proteomic analysis of lung adenocarcinoma identifies high HLA-DR expression to be associated with indolent tumor behavior

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Introduction
Lung adenocarcinoma (ADC) is a heterogeneous group of tumors associated with dramatically different survival rates, even when detected at an early stage. We hypothesized that a single cell proteomic approach would allow the dissection of cellular determinants of early lung ADC behavior.

We aim to ...

1. ADC mass cytometry panel captures the cellular diversity between ADC cell lines and PBMCs

Our ADC mass cytometry panel in ADC cell lines and PBMCs showed that dimensionality reduction and unsupervised computational analysis accurately capture the cellular diversity between and within different cell types (A) based on protein expression (B).

2. ADC antibody panel captures differences between indolent and aggressive lung ADCs

We tested our panel on 10 primary ADC human samples and identified major cell types (A). ADCs with long predicted survival (LPS) had a higher proportion of T cells (B). Epithelial clusters with high HLA-DR expression were positively correlated with T cell abundance (C-D).

3. Validation of mass cytometry data by spatial analysis suggests a role for HLA-DR in prognosis

We validated our CyTOF findings by immunofluorescence and spatial analysis, in which we showed that T cell abundance was positively correlated with HLA-DR expression in pan-cytokeratin+ cells (A) and that T cells in LPS samples were significantly closer to the first tumor cell in the space compared to short predicted survival (SPS) samples (B).

Conclusions & Future Directions

- Our results proved mass cytometry as a suitable tool to dissect ADC biology at the single cell level and to investigate the interplay between the TME and the epithelial compartment.
- We found an association between HLA-DR expression in epithelial cancer cells and T cell abundance, mainly in tumors with predicted indolent behavior, suggesting an immune response controlling tumor behavior.
- Future work will refine these results, integrate data from other platforms and determine whether the crosstalk of cancer cell subpopulations with specific subpopulations in the TME predicts tumor behavior.

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