Quantifying PD-L1 Spatial Distribution Signatures for Patient Selection Approaches

Flagship Biosciences Inc, Westminster, CO

Abstract

Infiltration of inflammatory checkpoints (e.g., PD-L1+ infiltrates) has demonstrated great promise in predicted and clinical trials. Thus, an understanding of spatial relationships is critical to stimulate or abrogate inflammatory responses against tumors by increasing expression of inflammatory checkpoint molecules. Unfortunately, spatial relationships in tissue sections pose significant challenges for a meaningful analysis in a pathological setting.

We have developed an approach to quantify spatial relationships in tissue sections. Infiltrating cells were visualized with CellPReS software to reveal 1) the total number of cells in the tumor/TME tissue compartments, and 2) the number of cells within distance ranges from the tumor/TME interface. This approach may be used to quantify inflammatory cell immune checkpoint expression across the tumor/TME interface. This proof of concept study demonstrated a unique correlation between the extent of PD-L1+ cell densities and the tumor/TME interface. The density of PD-L1+ cell densities across the tumor/TME interface may provide an approach to stratify patients.

Materials and Methods

- Immunohistochemistry staining for PD-L1 (22C11, DAKO) was performed and CellPReS software was used to assess inflammatory cell distributions in the whole tissue sections.
- PD-L1+ cells were spatially calculated relative to: 1) the total number of cells in the tumor/TME tissue compartments, and 2) the total number of cells within a distance from the tumor/TME interface.
- PD-L1+ cell densities were calculated across an entire tissue section.

Results

- Interestingly, several unique PD-L1+ distribution patterns relative to the tumor/TME interface were observed in the sample study analyzed.

Application of the Approach

- Whole Slide Image
- Cell Parameters
- Cell Feature Comparison
- Cell Type Classification
- Target Cell Measurements
- Data Mining

Conclusion

- This study provided a novel method for assessing inflammatory checkpoint cell type spatial distributions relative to a tissue feature, the tumor/TME interface.
- The data suggested that unique spatial patterns of inflammatory cell type distributions could be used to identify unique patient populations compared to existing stratification methods.
- Taken together, the proposed approaches demonstrate a unique quantitative assessment of inflammatory cell infiltrates in tumors that could be used to gain insights into inflammatory cell type distributions and interactions in tumors, inflammatory cell spatial responses to oncology therapies, and novel patient sub-group identification for traditional and immunotherapeutic interventions.