



P3.143: Single cell spatial analysis identifies COL10A1+CAF Treg Interaction driving immunosuppression in Micropapillary lung adenocarcinoma

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INTRODUCTION

Micropapillary lung adenocarcinoma (MIP) is a high-risk histologic phenotype associated with early recurrence and poor survival, yet the microenvironmental basis of its aggressive behavior remains poorly understood.

The stromal and immune architecture surrounding micropapillary components, particularly spatially organized niche programs linked to adverse outcomes, remains incompletely defined.

Objective: Define the stromal–immune architecture of MIP and identify adverse spatial niche programs.

METHODS

Cohort Design:

We enrolled 154 LUAD patients with micropapillary components and 154 matched controls without micropapillary components. Controls were matched 1:1 by sex, age, and TNM stage.

Single-cell profiling:

Single-cell RNA sequencing was performed on 109,416 cells from 6 tumors with micropapillary components, 6 tumors without micropapillary components, and 12 adjacent normal lung tissues. Integrated analysis was used to characterize tumor, stromal, and immune cell populations associated with micropapillary components.

Spatial validation:

Spatial analysis and multiplex immunofluorescence were used to validate the spatial colocalization of key stromal and immune cell populations.

DISCUSSION AND CONCLUSION

Actionable Take Away Message

- Micropapillary LUAD is characterized by a distinct immunosuppressive stromal–immune state.
- COL10A1+ CAFs and FOXP3+ Tregs are enriched and spatially co-localized in micropapillary-containing regions, consistent with an immune-excluded niche.
- This stromal–immune program is associated with immune exclusion and poor prognosis.

Micropapillary histology was associated with significantly worse DFS (HR=3.528, P<0.0001) and OS (HR=2.209, P=0.0061).

Future Direction for Research

- Validate the COL10A1+ CAF–FOXP3+ Treg niche in larger independent cohorts.
- Investigate ERG and LAMA4–CD44 signaling as potential therapeutic vulnerabilities.
- Explore COL10A1+ CAF-targeted strategies to reverse immune exclusion.

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Artificial Intelligence (AI) Use Disclaimer:

During preparation of this manuscript, the authors used OpenAI Codex to support English-language editing, manuscript organization, and reference-record verification. The authors reviewed and edited the output and take full responsibility for the content of the manuscript.

RESULTS

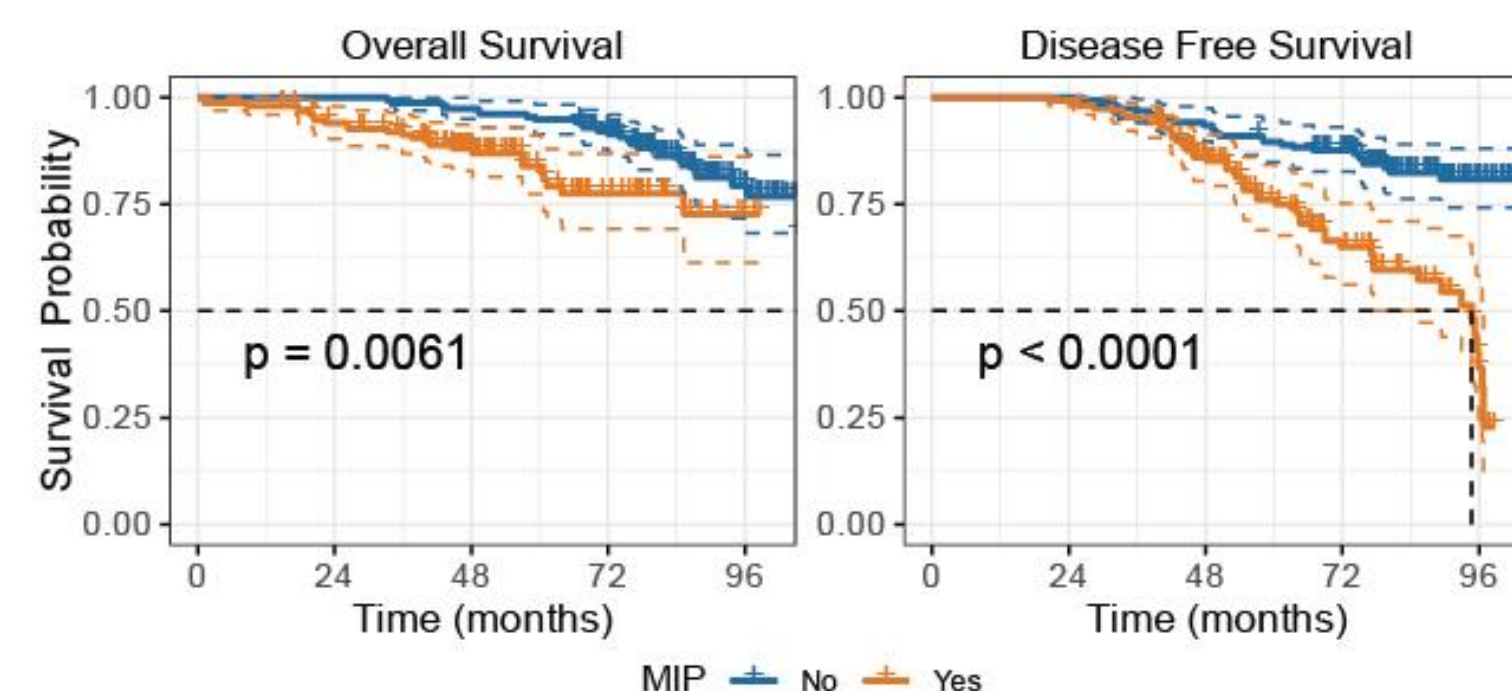


Figure 1. Kaplan–Meier curves for overall survival and disease-free survival in the clinical cohort.

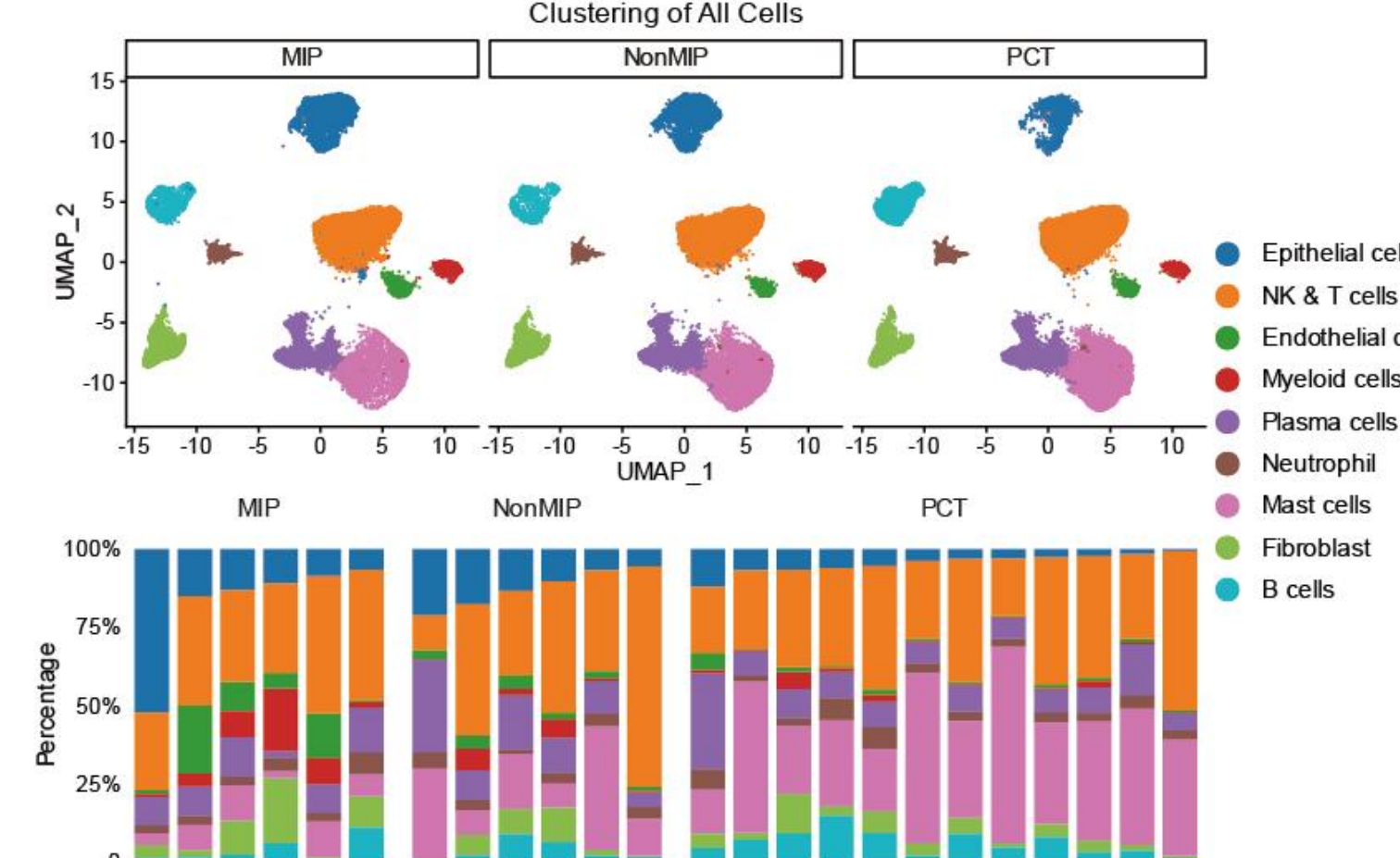


Figure 2. UMAP visualization of 109,416 cells from micropapillary (MIP) tumors, non-micropapillary (NonMIP) tumors, and paracancerous tissues (PCT)

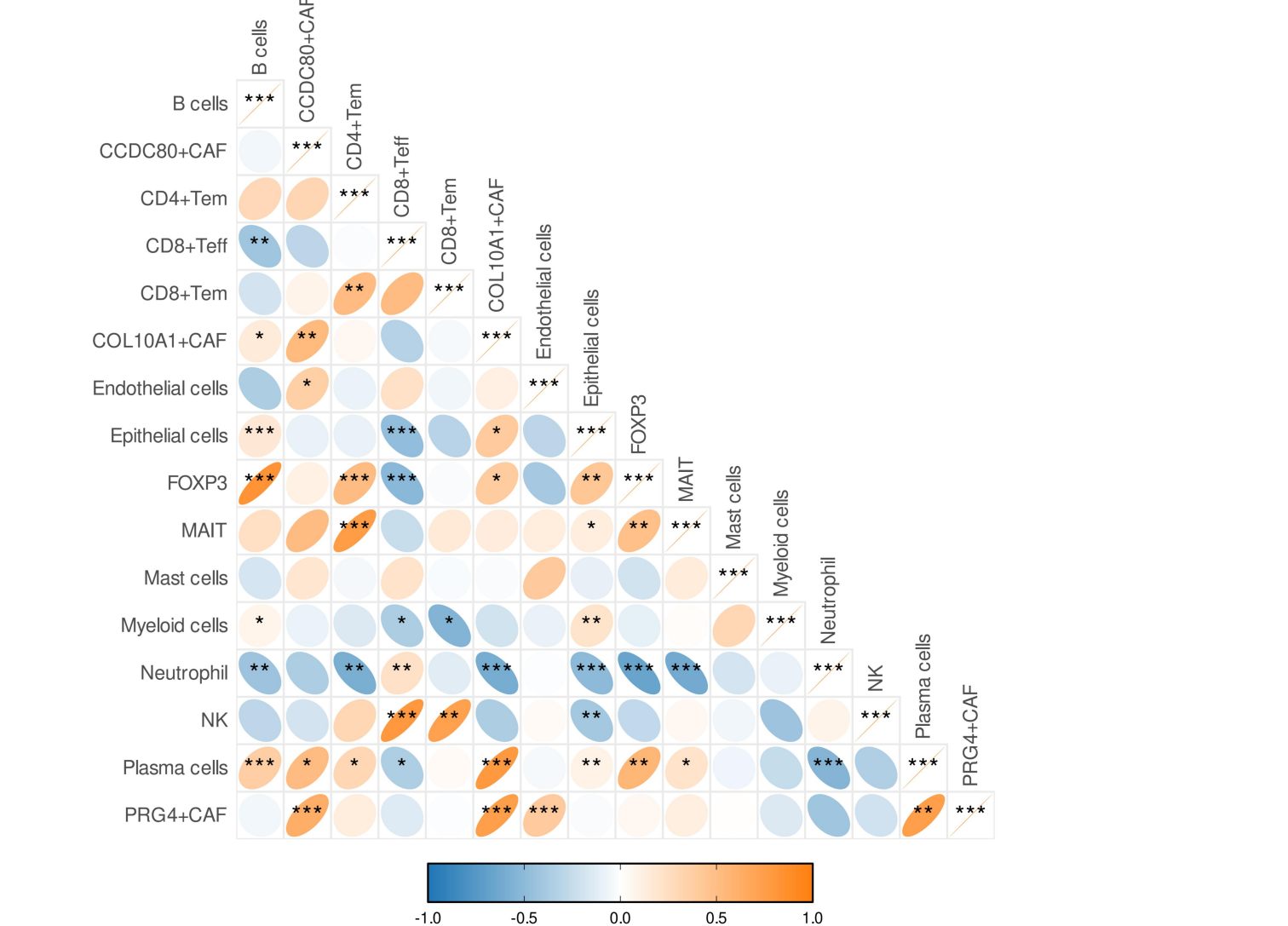


Figure 3. Heatmap displaying the correlations across all cell types in the single-cell data

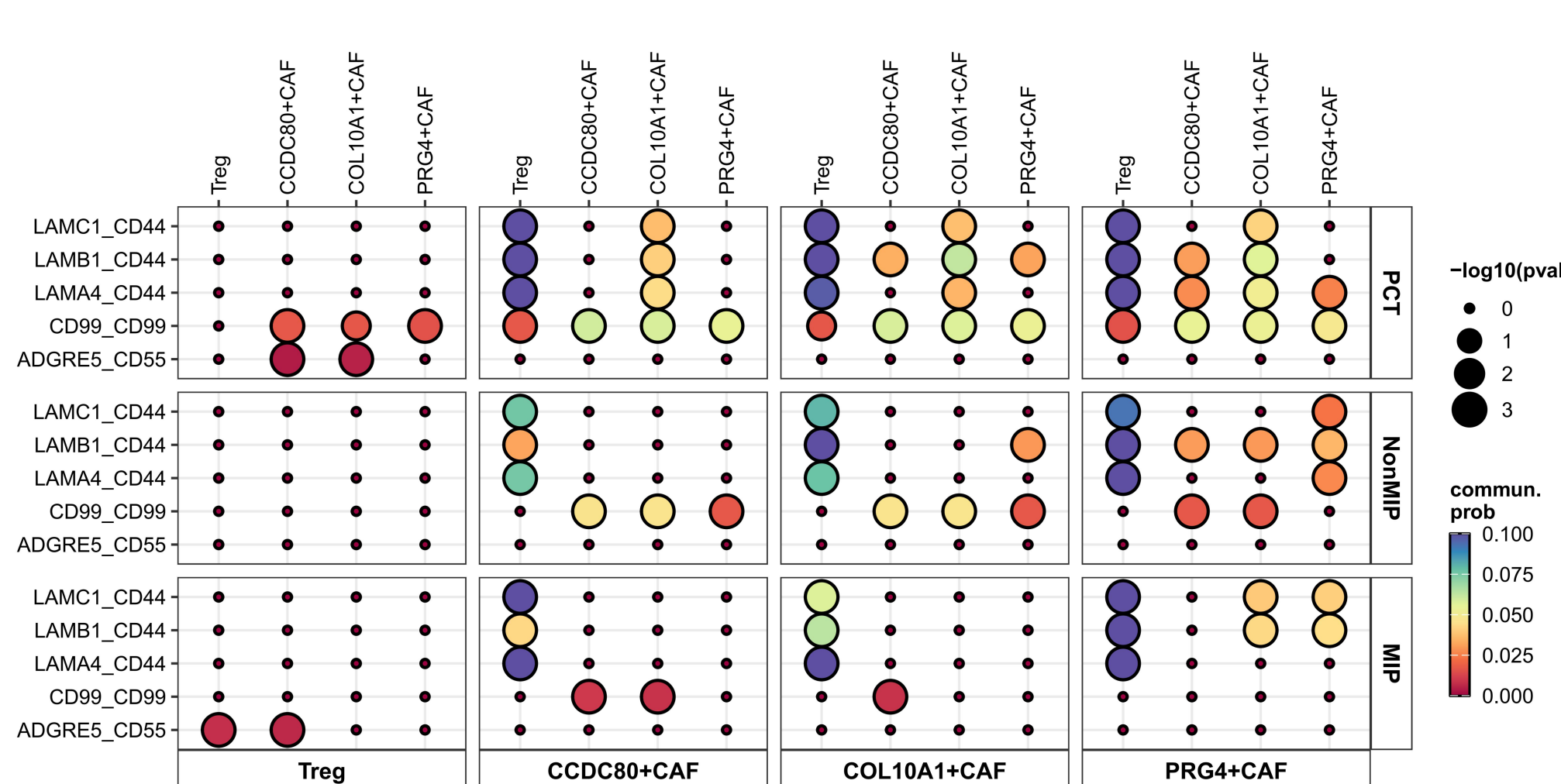


Figure 6. CellChat analysis of Treg–CAF interactions across PCT, NonMIP, and MIP LUAD regions.

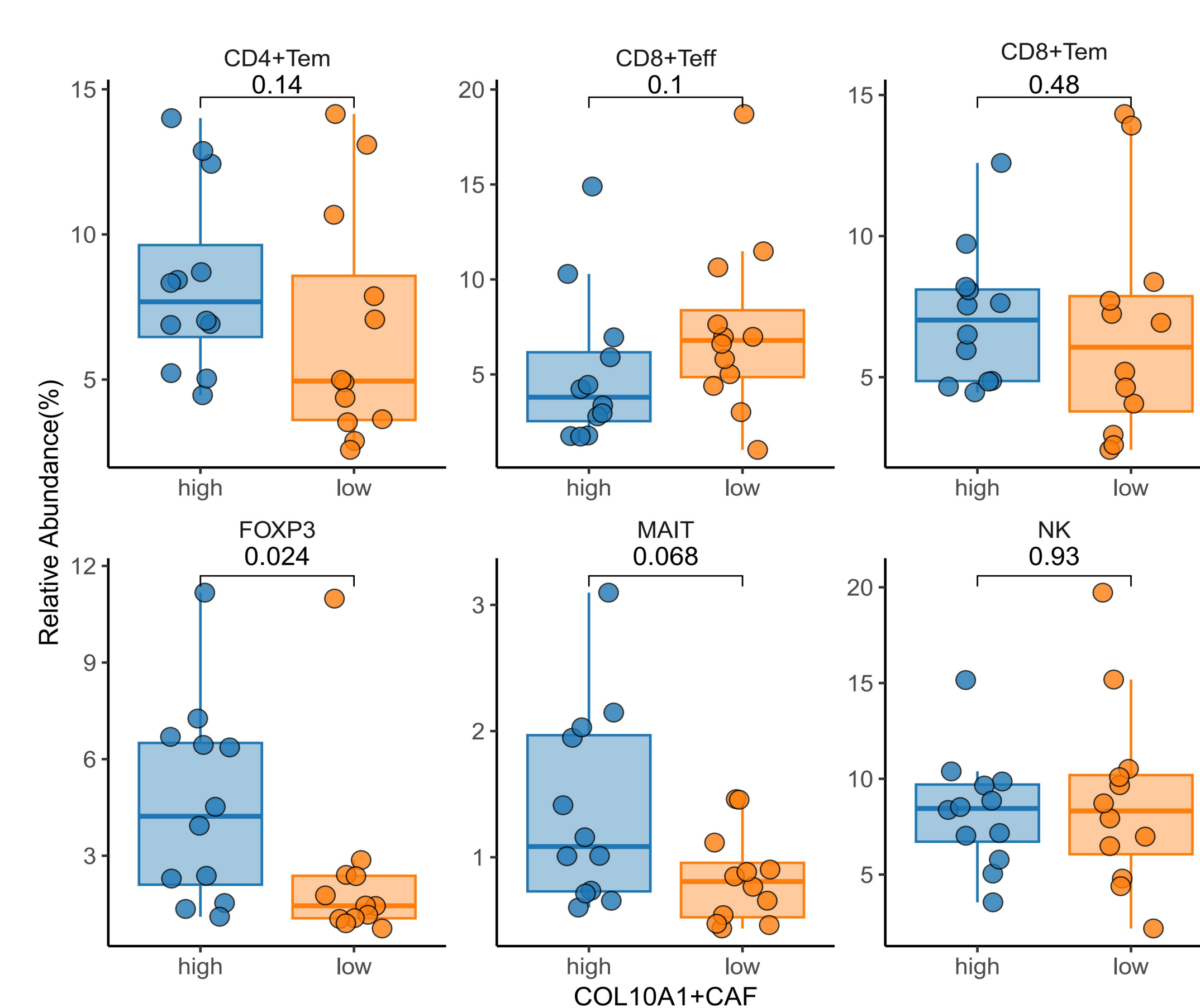


Figure 4. Relative abundances of CD4+ Tem, CD8+ Teff, CD8+ Tem, FOXP3+ Treg, MAIT, and NK cells in tumors with high or low COL10A1+ CAF abundance.

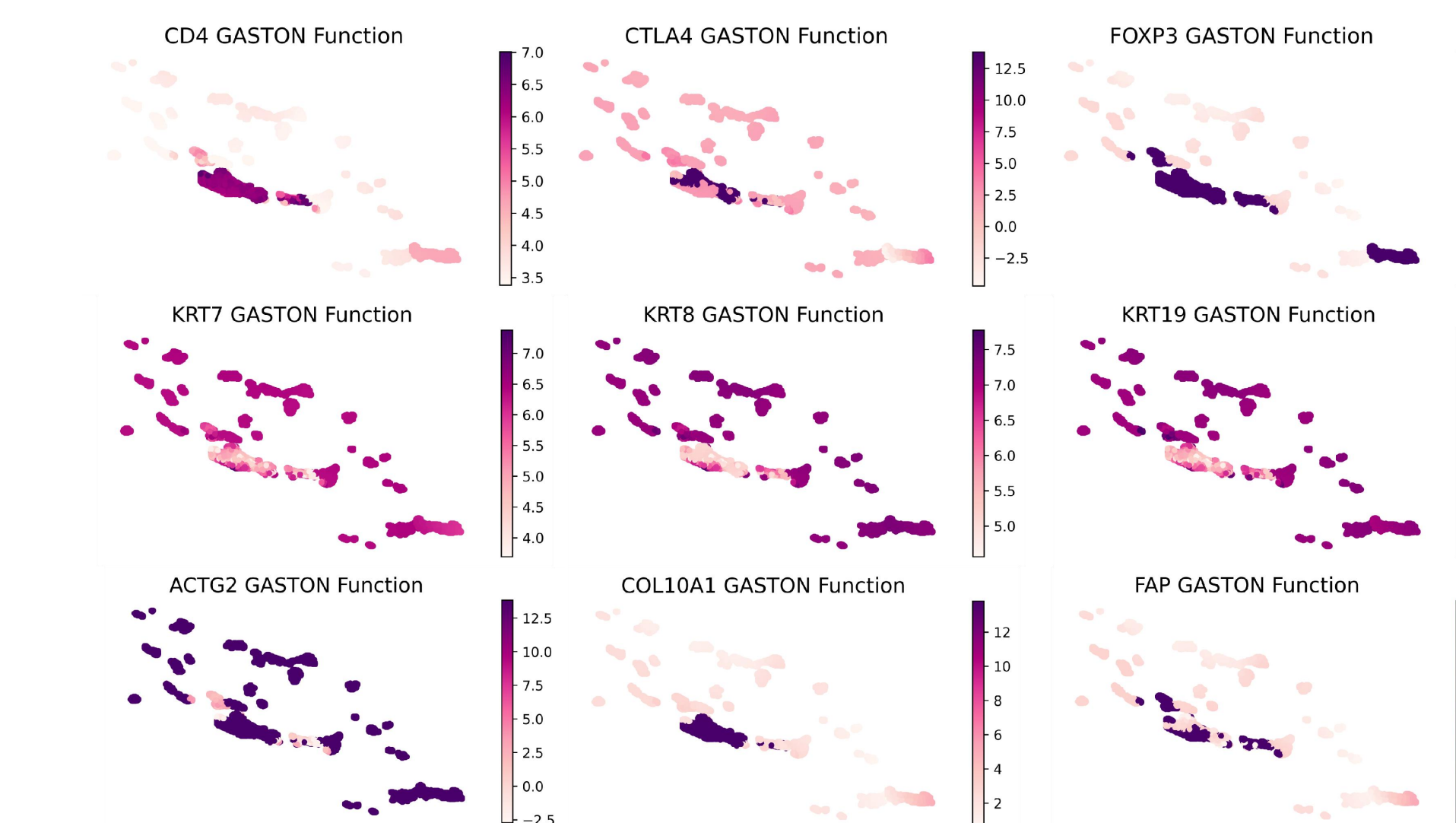


Figure 5. Spatial maps of GASTON-derived function scores for Treg-associated markers, fibroblast markers, and epithelial markers in MIP-predominant tissues.

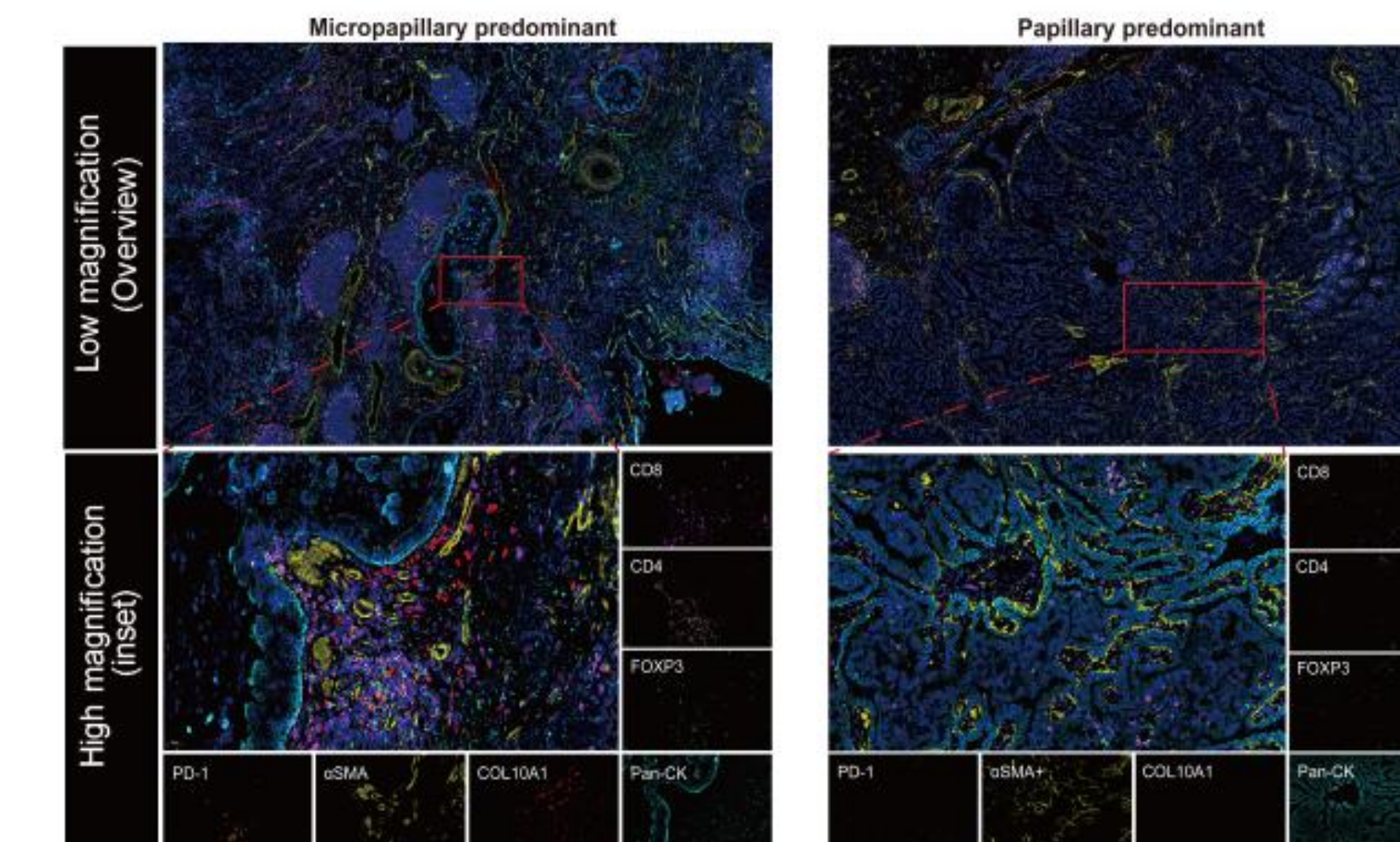


Figure 7. Representative multiplex immunohistochemistry images of micropapillary and papillary LUAD stained for Pan-CK, COL10A1, α-SMA, CD4, FOXP3, CD8, and PD-1.