

Spatial Multi-omics and AI-Driven Digital Pathology Identify Determinants of Pathological Response to Neoadjuvant Chemo-IO in NSCLC

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STUDY SNAPSHOT

55

patients analyzed

60%

major response rate (pCR or MPR)

100%

known pathologic outcome

50

evaluable surgical AI data

BACKGROUND

Neoadjuvant chemo-immunotherapy improves outcomes in resectable NSCLC, yet the biological and spatial determinants of pathological complete response (pCR) remain poorly understood. Robust biomarkers of response are needed to inform post-surgical management, including the potential need for adjuvant therapy.

Integrating AI-based digital pathology with spatial transcriptomic and proteomic profiling offers the opportunity to resolve tumor-immune-stromal organization beyond conventional morphology and to identify cellular interactions and spatial features associated with pathological response (pR).

MULTIMODAL METHODS

AI DIGITAL PATHOLOGY
Lunit SCOPE IO was applied to whole-slide H&E images to quantify tumor architecture, immune infiltration, stromal organization, and tertiary lymphoid structures (TLS).

SPATIAL OMICS
10x Genomics Visium spatial transcriptomics and COMET high-plex spatial proteomics were used to characterize tumor, immune, extracellular matrix, and fibroblast programs at spatial and cell-resolved levels.

MULTIMODAL INTEGRATION
AI-derived tissue features were integrated with spatial transcriptomic and proteomic profiles and associated with residual viable tumor and pathological response (pR).

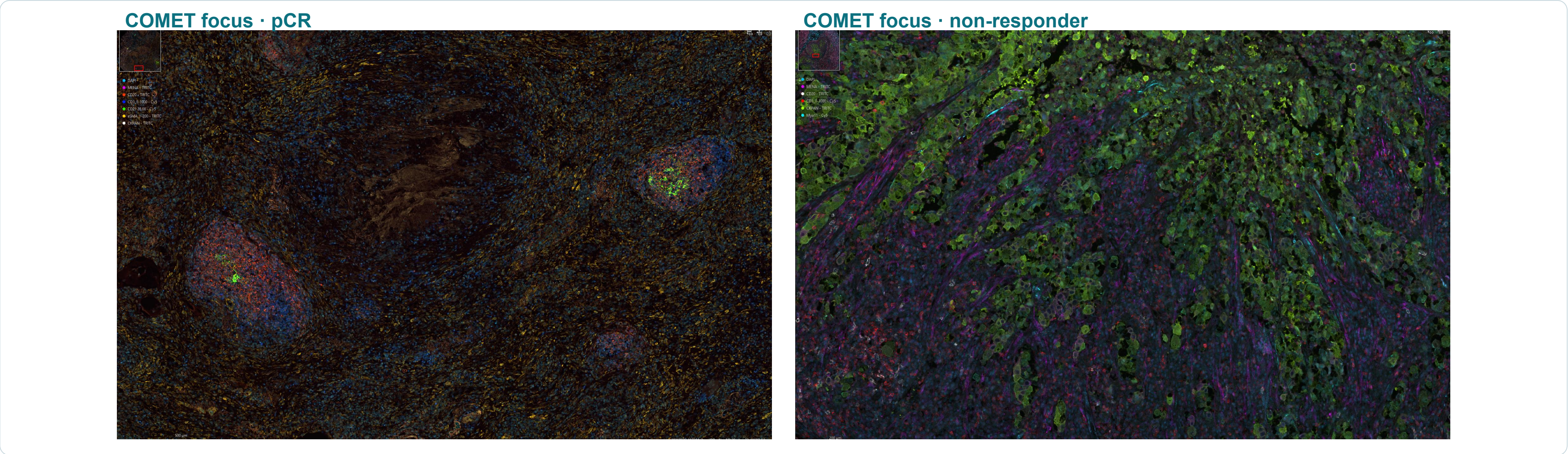
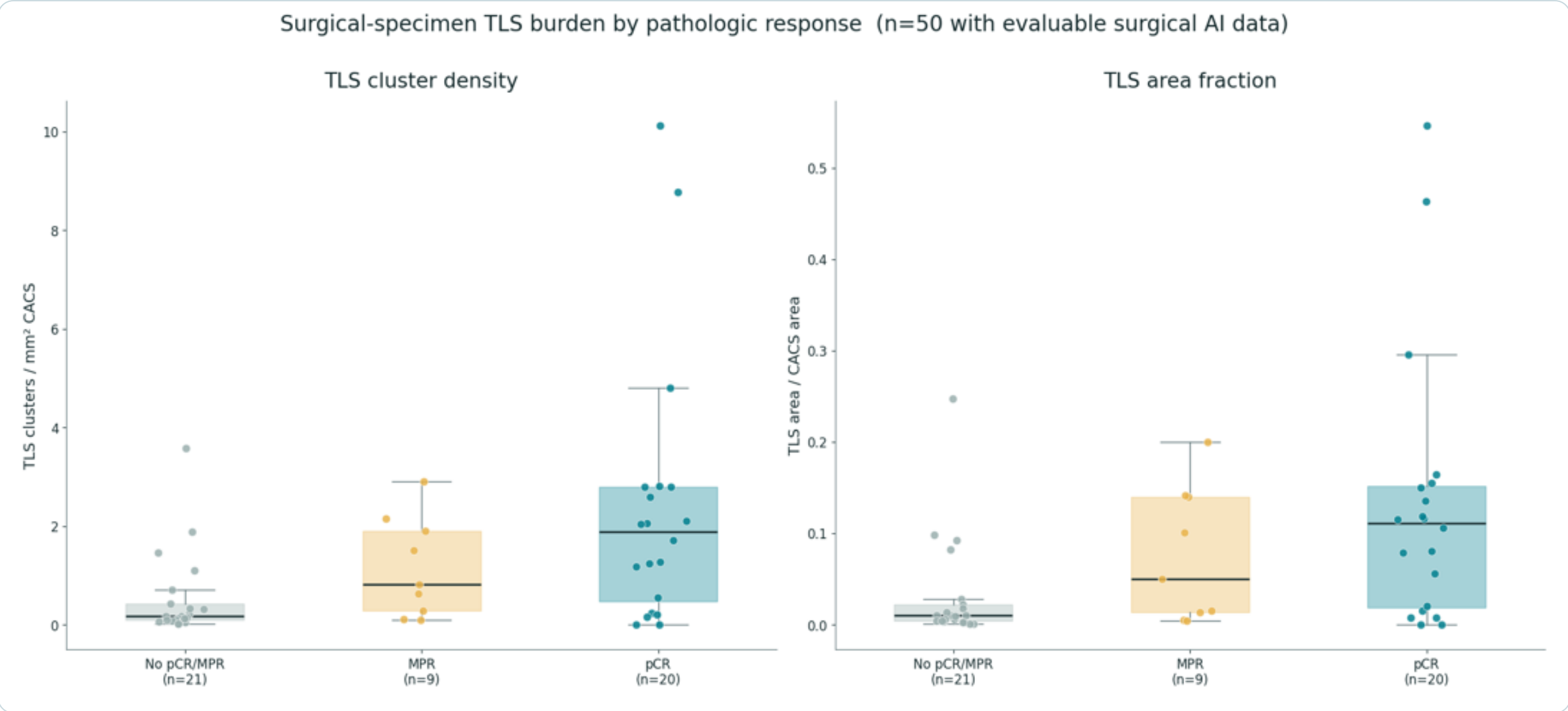
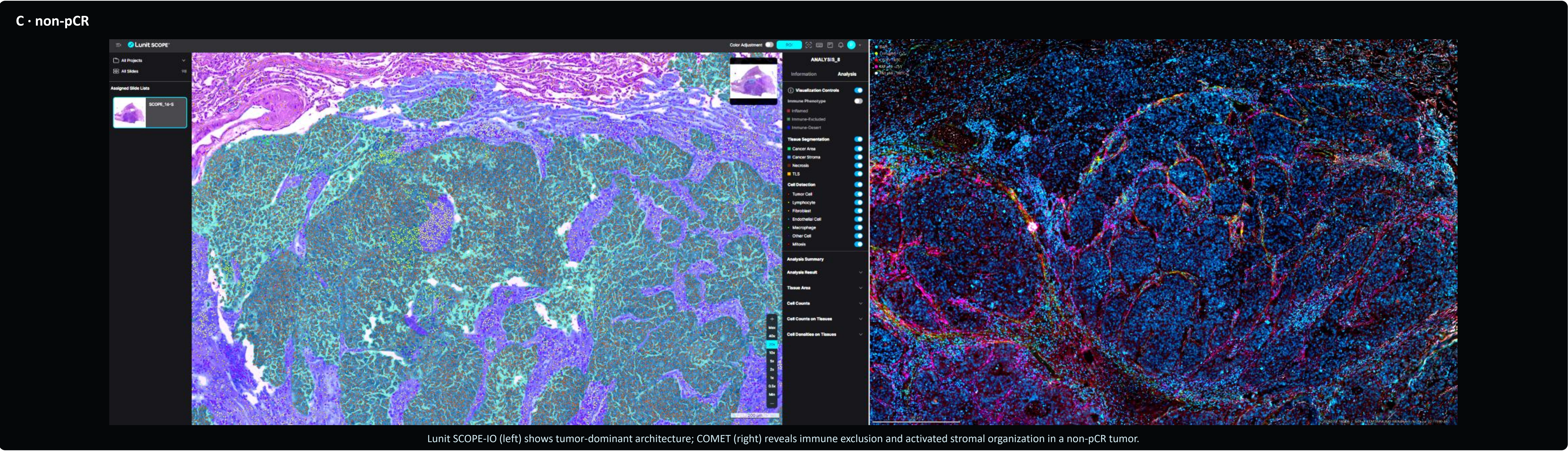
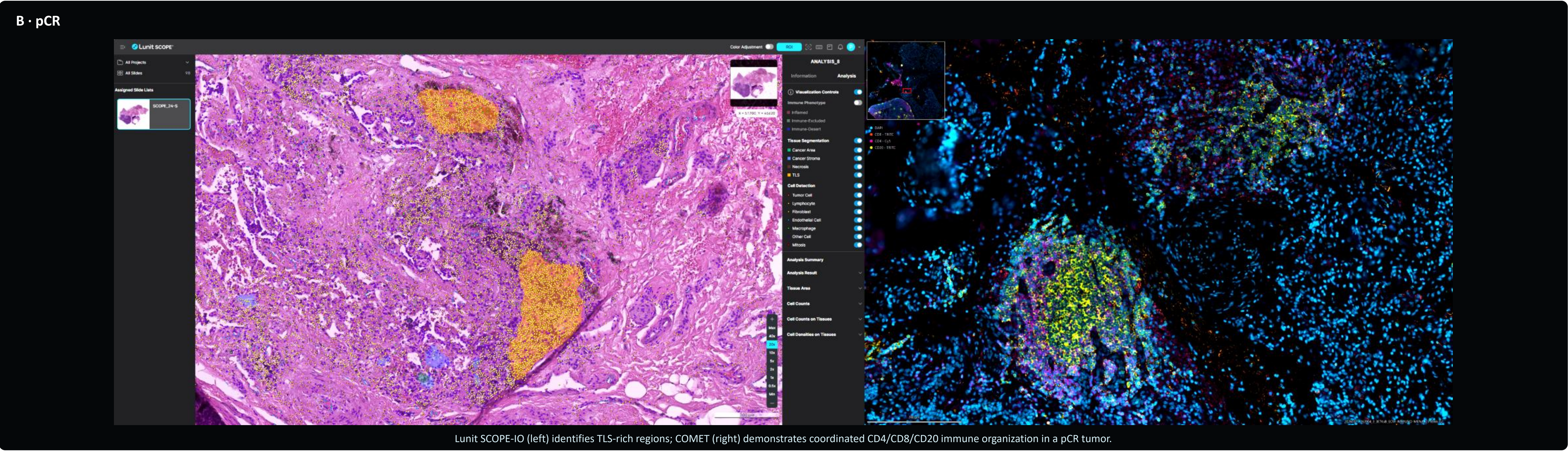
KEY FINDINGS

- Residual viable tumor was positively associated with TLS cluster density. TLS preferentially localized within organized post-treatment stromal compartments, with a trend toward a positive association.
- pCR tumors displayed an inflamed and spatially organized microenvironment characterized by prominent TLS.
- In contrast, non-pCR tumors exhibited an immune-excluded architecture, increased tumor-cell proliferation, and enrichment of pro-tumoral cancer-associated fibroblasts (CAFs).

CONCLUSION

AI pathology plus spatial omics reveals distinct immune-stromal tissue architecture associated with pCR and suggest the development of spatially resolved biomarkers for post-surgical treatment decisions.

FIGURE 1 Paired AI pathology and spatial proteomics expose divergent response ecosystems



References: 1. Melchiorre R, Di Modugno F, Di Carlo A, D'Ambrosio L, Palermo B, Tucci A, Paoletti F, Sperduti I, Campo G, Tajiri R, Gallina F, Visca P, D'Andrea D, Nisticò P. Reciprocal regulation of mTENA and TGF-β signaling in cancer-associated fibroblasts promotes EMT, immunosuppression, poor prognosis, and ICT resistance in NSCLC. *J Immunother Cancer*. 2026 Jan 27;14(1):e013098. 2. Porciello N, Gallina F, Frittullo G, Fusco F, D'Ambrosio L, Balzano V, De Nicola F, Visca P, Landi L, Cappuzzo F, Nisticò P. Spatial transcriptomics highlights B cells as key contributors to a complete and durable response to chemo-immunotherapy in a patient with resectable NSCLC. *J Immunother Cancer*. 2025 May 11;13(5):e011563.