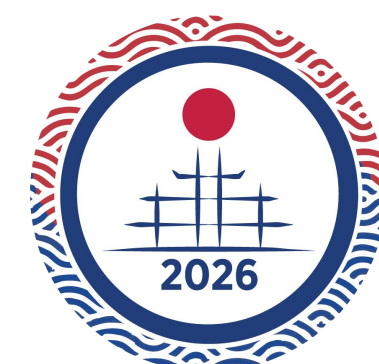




P2.149: A TPX2 High Tumor Program Defines Resistance to Neoadjuvant Chemoimmunotherapy in Resectable Stage III NSCLC

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INTRODUCTION

Neoadjuvant chemoimmunotherapy (NCIT) is an established treatment strategy for resectable stage III NSCLC, but many patients do not achieve major pathologic response (MPR) and remain at high risk of recurrence.

Biomarkers that capture resistance and improve risk stratification are needed.

We investigated whether TPX2 marks a resistant tumor cell state associated with adverse outcomes after NCIT

METHODS

Design:

Public single-cell RNA sequencing and spatial transcriptomic datasets from NCIT-treated NSCLC tumors were integrated to identify response-associated tumor programs and their spatial immune contexture.

Validation:

Key findings were validated by multiplex immunofluorescence. TPX2 protein expression was assessed by immunohistochemistry in an independent cohort of 46 patients with resectable stage III NSCLC treated with NCIT followed by surgery.

Outcome analysis

Associations with pathologic response, disease-free survival (DFS), and overall survival (OS) were evaluated. Multivariable Cox models including MPR status and TPX2 expression were constructed in the 46-patient validation cohort.

DISCUSSION AND CONCLUSION

Actionable Take Away Message

- TPX2-high tumor cells define an NCIT-resistant tumor state.
- TPX2-high regions spatially colocalize with MARCO+ myeloid cells, consistent with a suppressive niche.
- High TPX2 is associated with non-MPR and inferior survival, with prognostic value beyond MPR.

TPX2 remained independently associated with DFS beyond MPR (P=0.032), with lower DFS event risk in TPX2-negative patients (HR=0.20, 95% CI: 0.05–0.87).

Future Direction for Research

- Validate TPX2 as a biomarker for risk stratification beyond pathologic response in larger multicenter cohorts.
- Investigate the TPX2-high tumor–MARCO+ myeloid niche as a potential therapeutic target for NCIT resistance.

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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

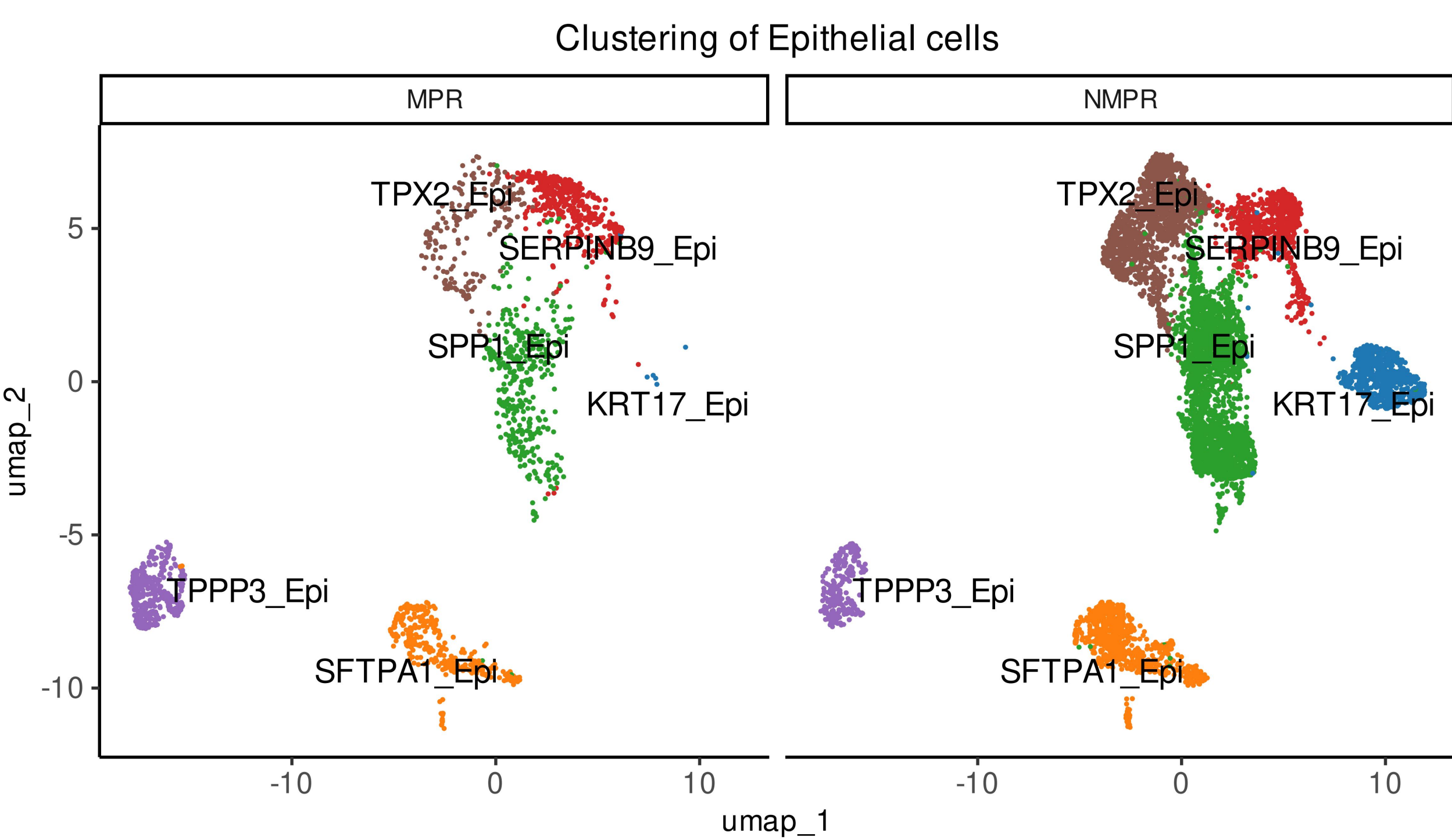


Figure 1. UMAP visualization of epithelial cell subclusters and their distribution across MPR and NMPR groups

Tissue distribution

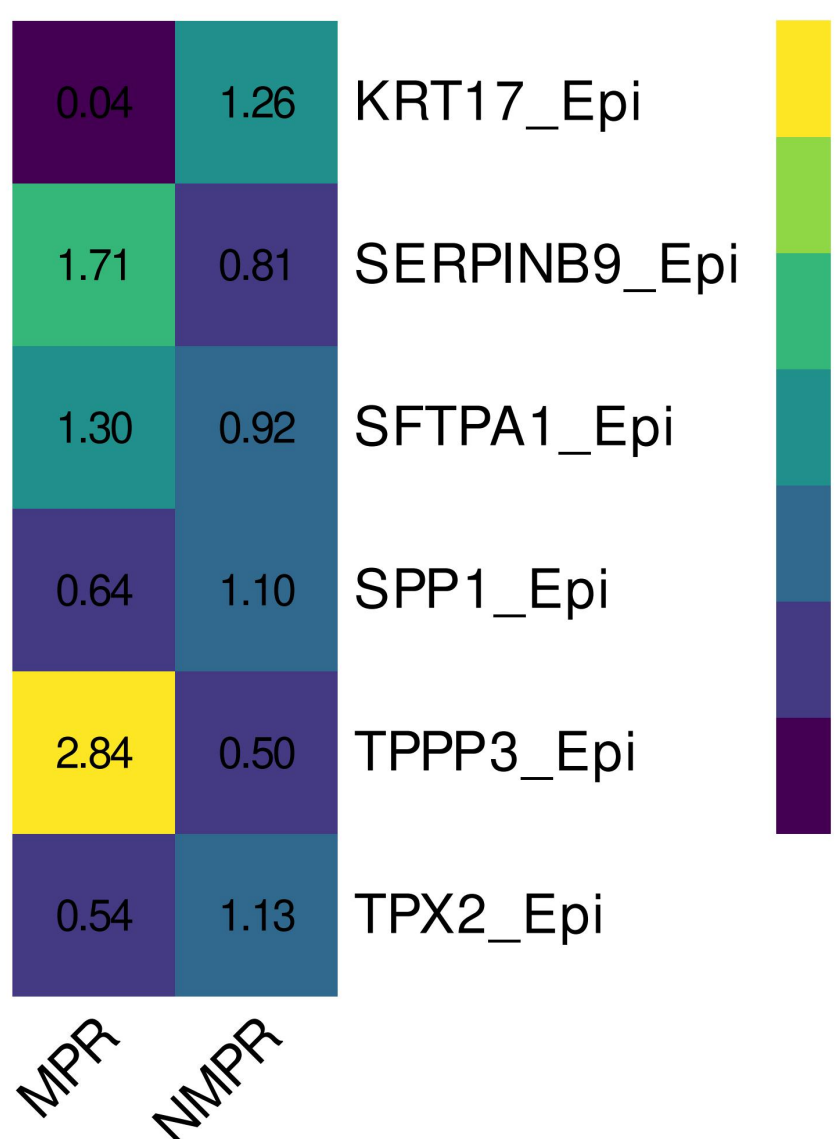


Figure 3. Ro/e heatmap showing enrichment or depletion of epithelial subclusters

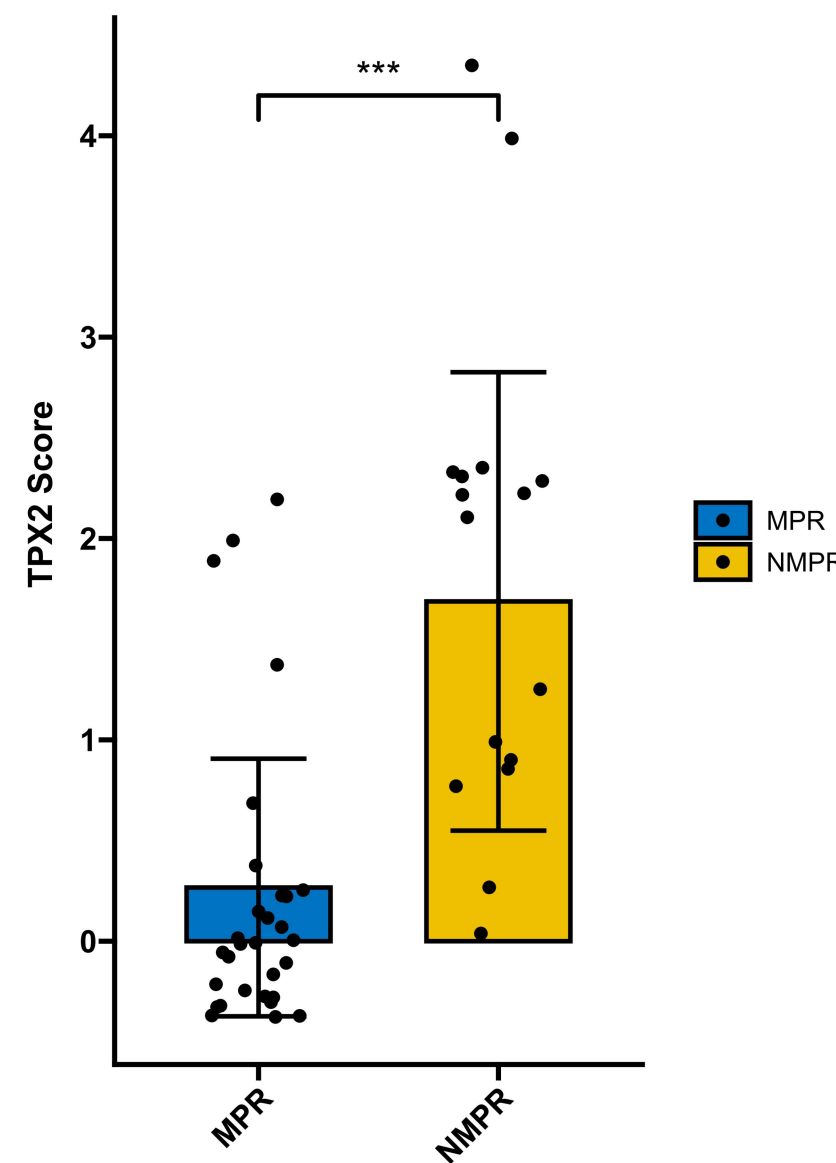


Figure 4. Quantitative comparison of TPX2 protein expression in MPR and NMPR tumors

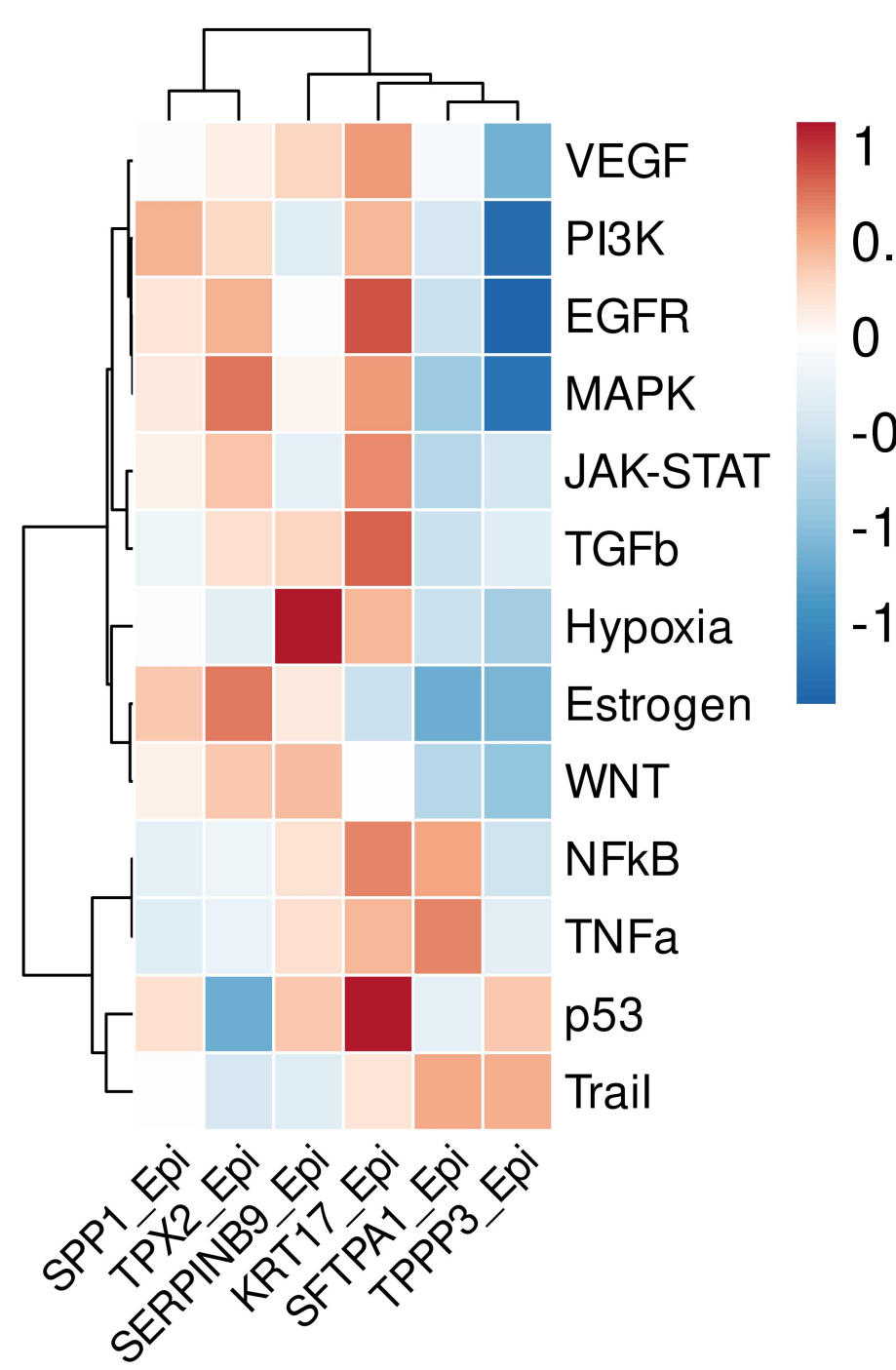


Figure 2. Pathway activity heatmap showing activation of cancer-related signaling pathways

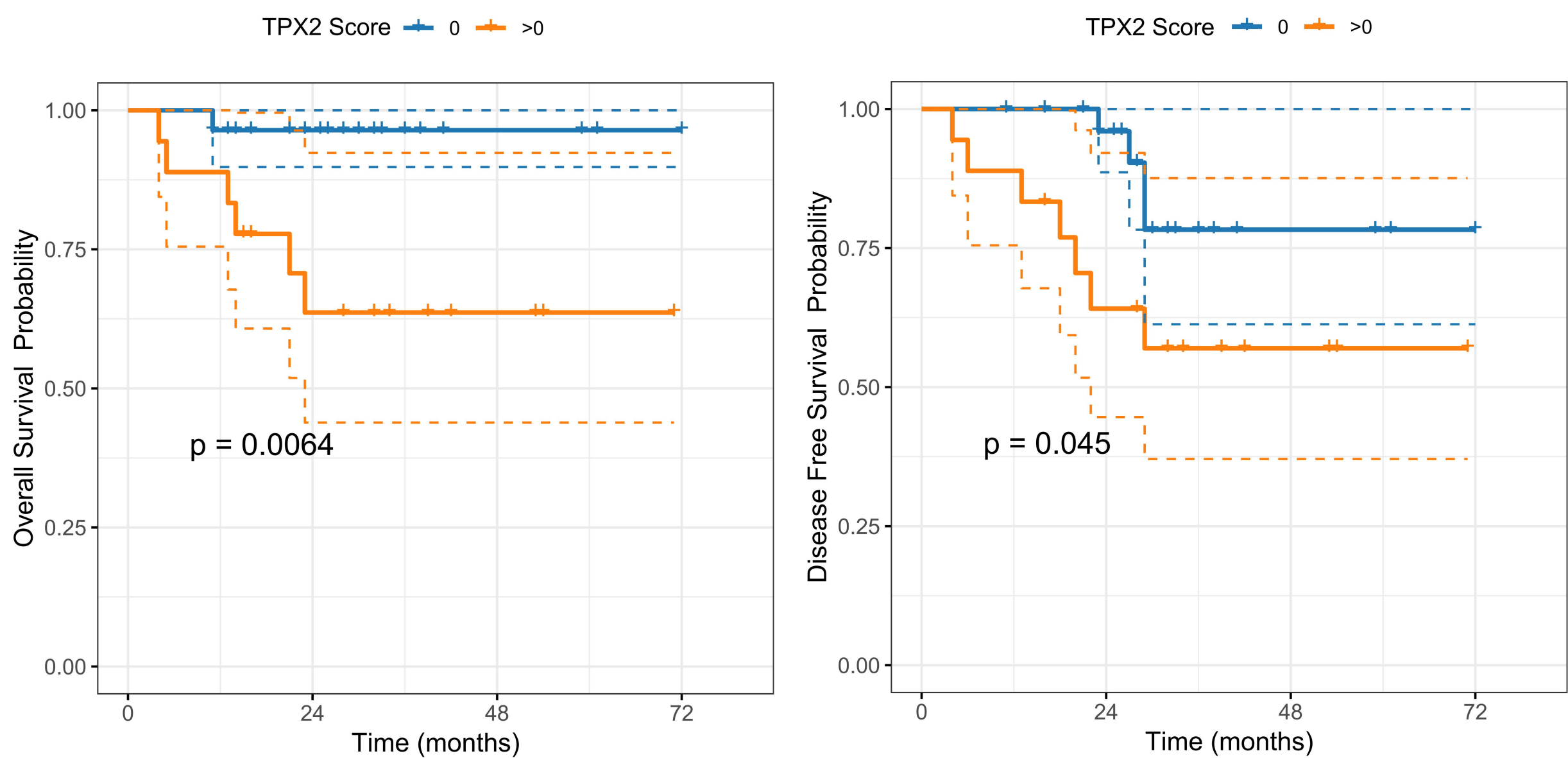


Figure 5. Exploratory Kaplan-Meier curves for overall survival and disease-free survival stratified by TPX2 IHC score in surgical resection specimens.

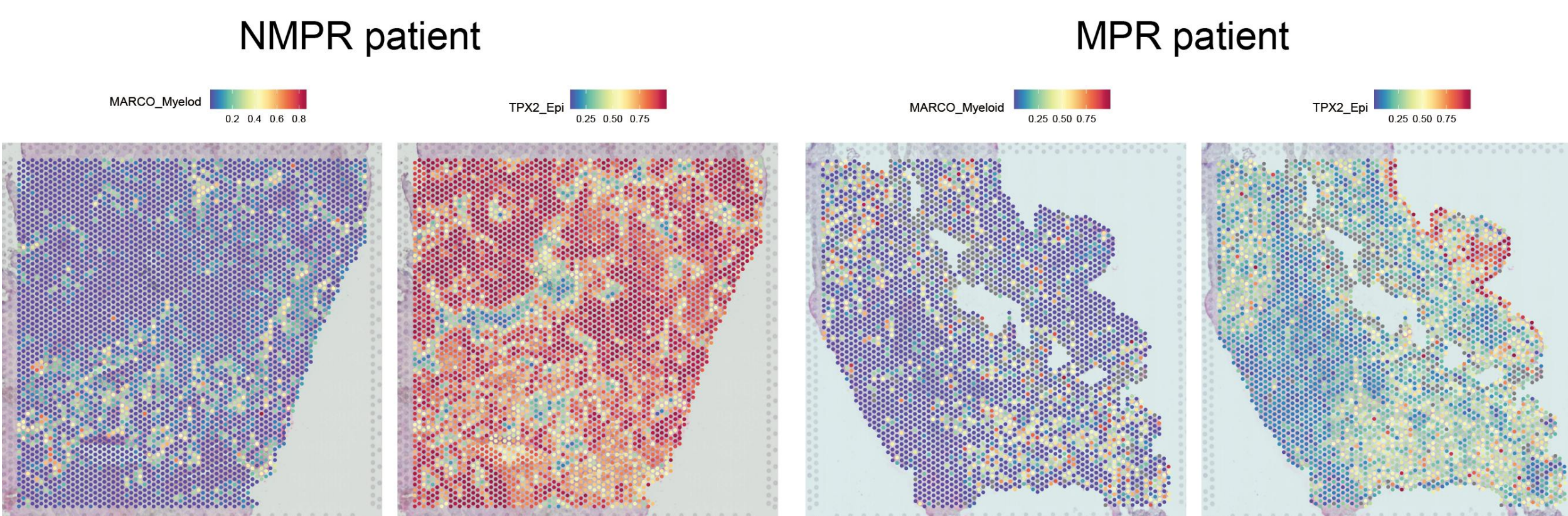


Figure 6. Spatial transcriptomics analysis shows co-localization of epithelial and proliferating cells in the NMPR group, whereas no co-localization is observed in the MPR group.