Comprehensive assessment of unfolded protein response and its association with tumor progression in pan-cancer.

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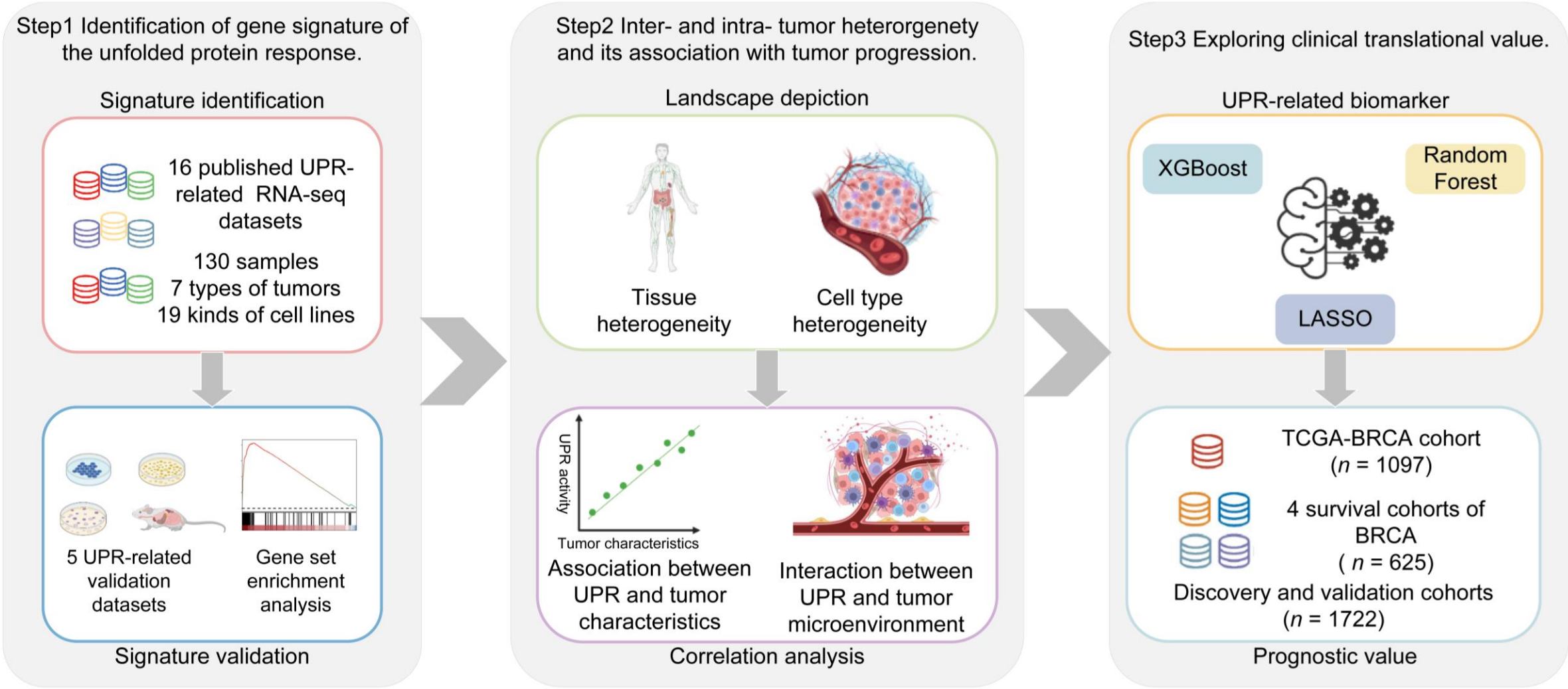
Introduction

This study proposes an unfolded protein response (UPR) gene signature, reveals the heterogeneity of UPR activity at the pan-cancer level, and identifies prognostic biomarkers associated with breast cancer.

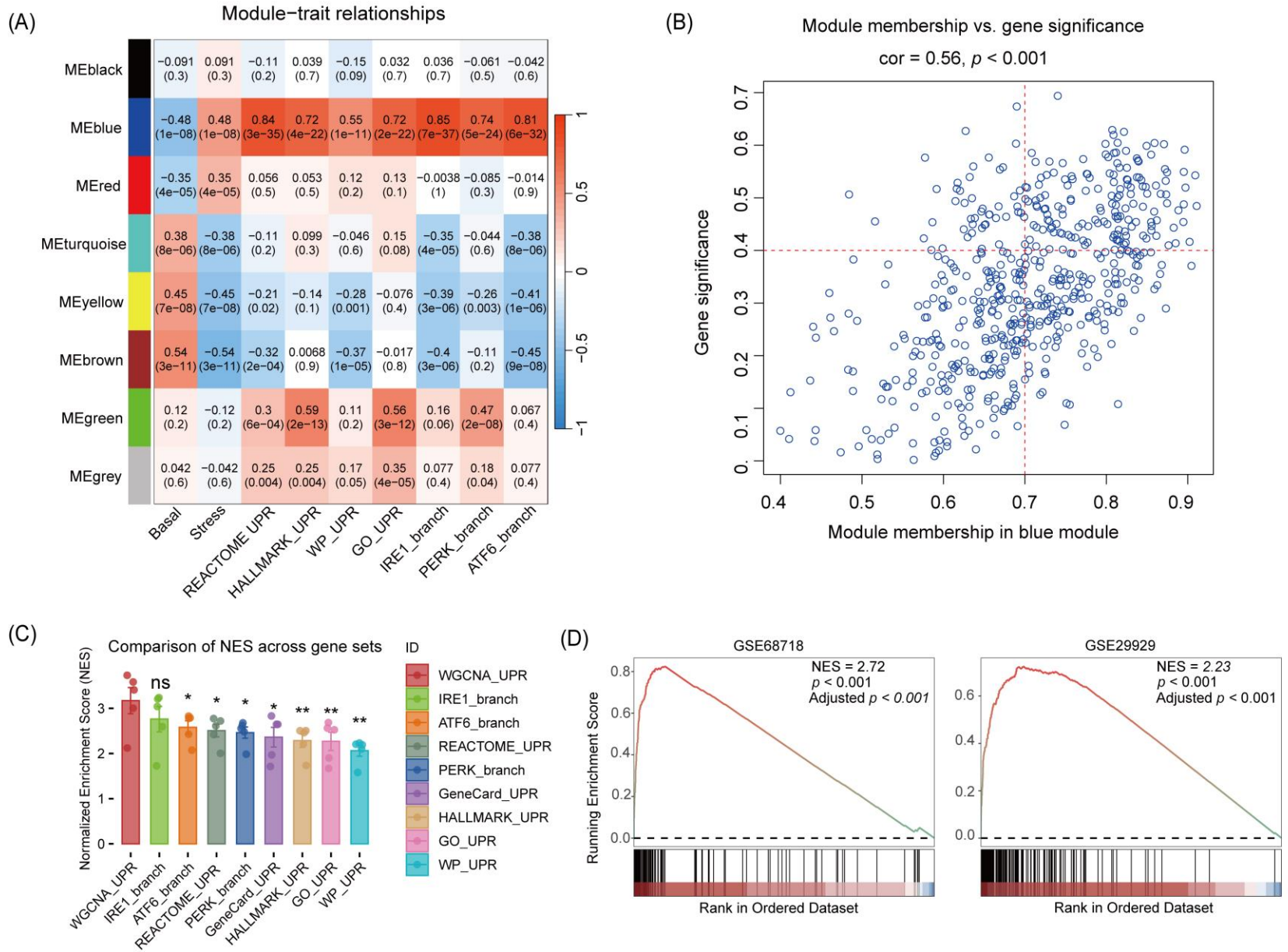


Highlights

- Developed a transcriptome-based unfolded protein response (UPR) signature that enables reliable assessment of UPR activation across pan-cancer.
- Systematically characterized the landscape of UPR heterogeneity and uncovered its multidimensional associations with key tumor features.
- Identified and validated a UPR-related biomarker with significant prognostic value in breast cancer.

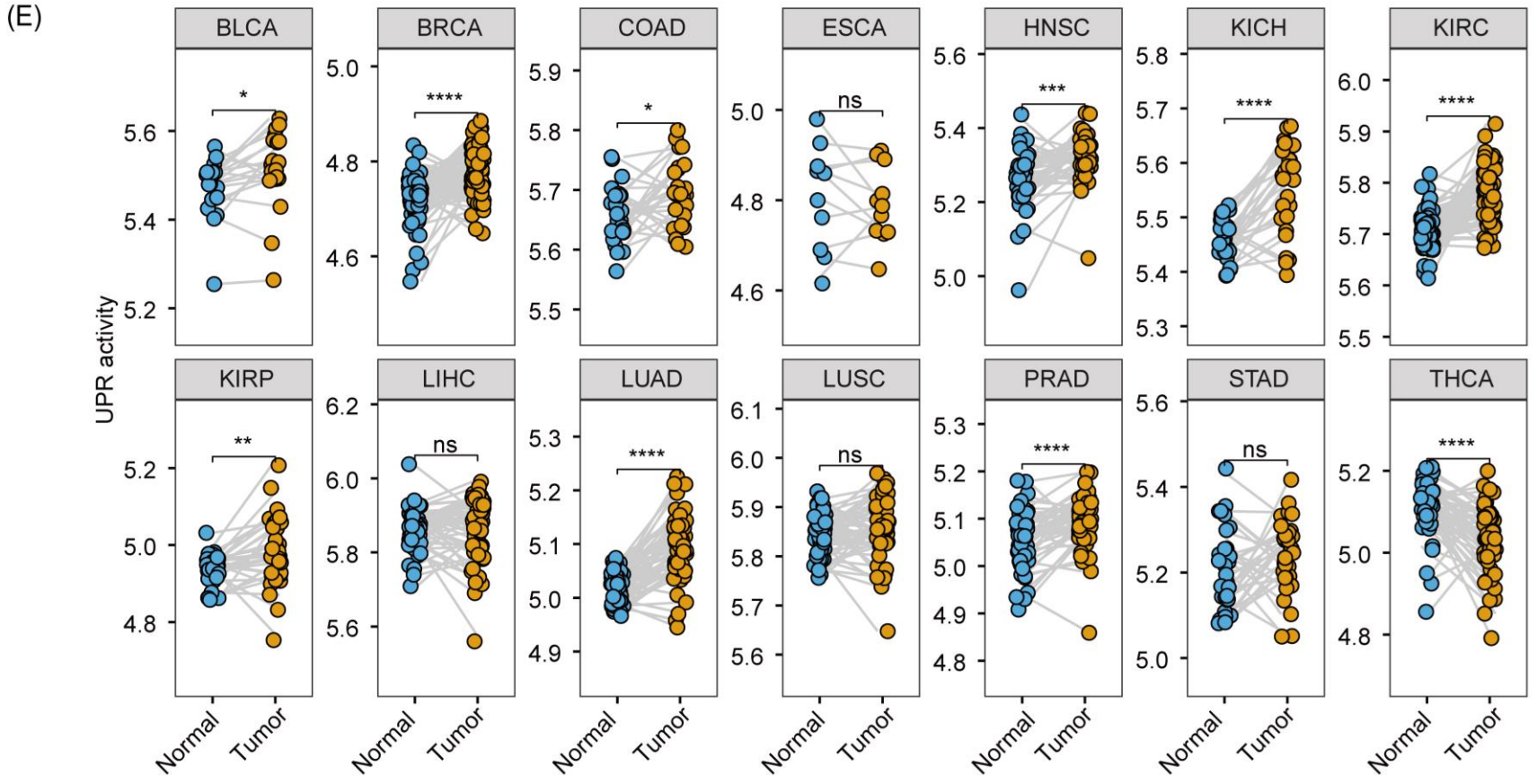
Results

Identified and validated gene signatures for assessing UPR status in tumors.



Results

UPR is broadly activated in tumor tissues, particularly in breast cancer, prostate cancer, and other cancer types.



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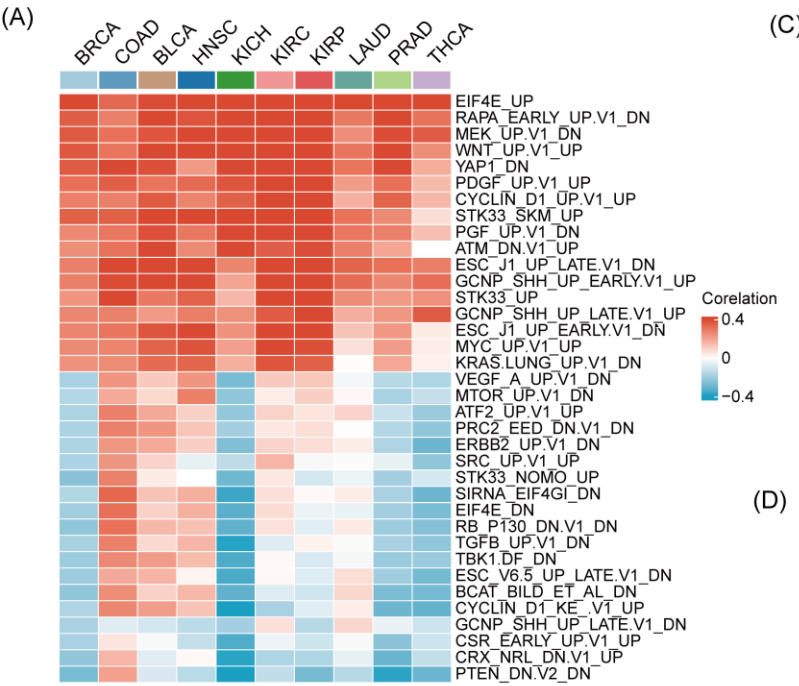
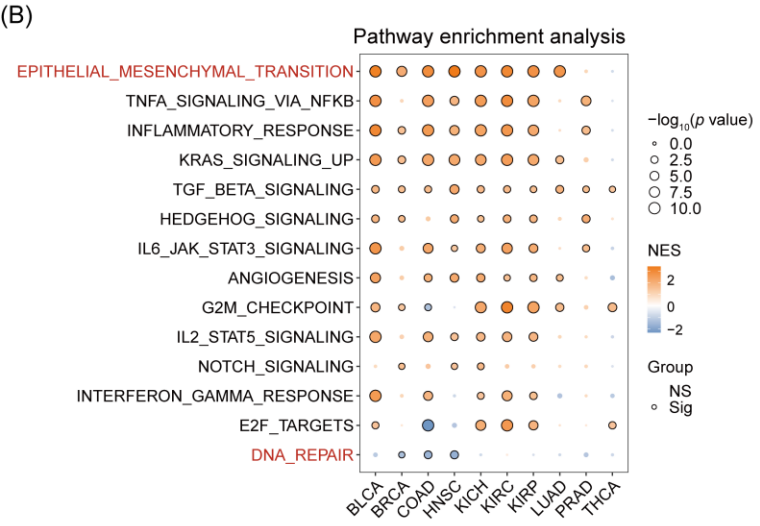
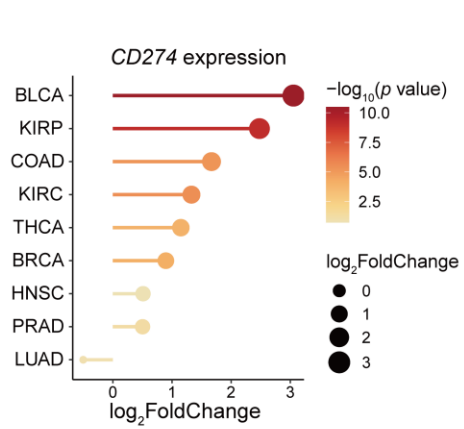
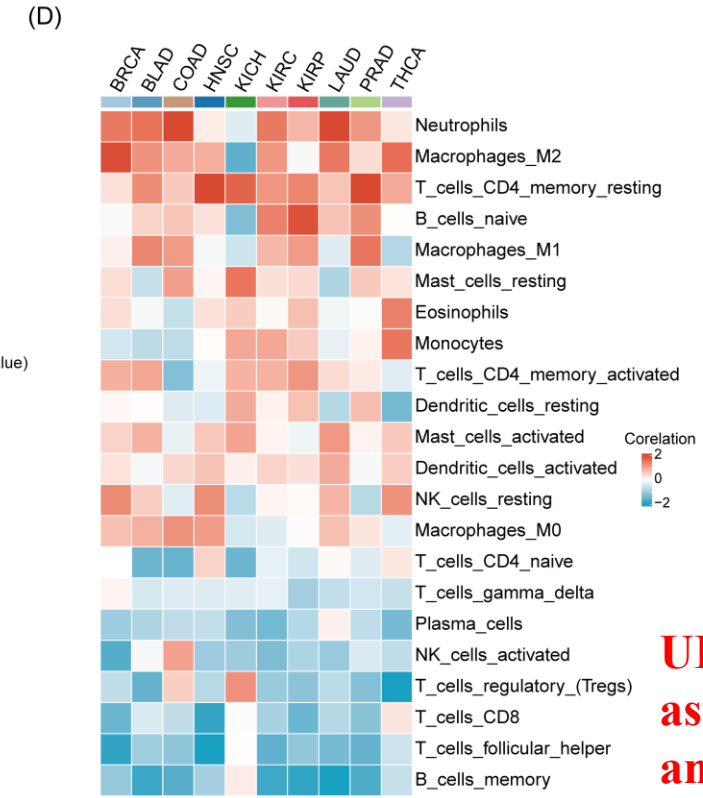
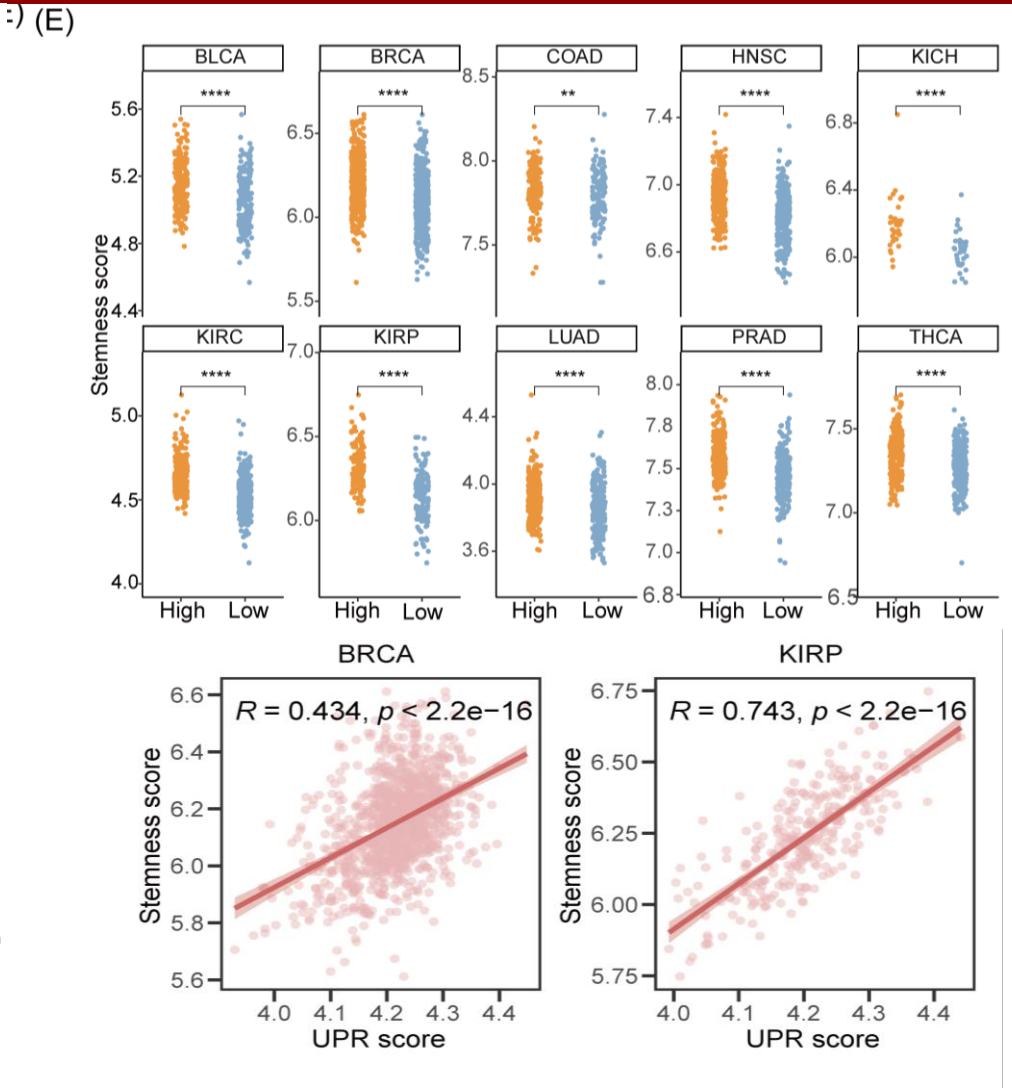






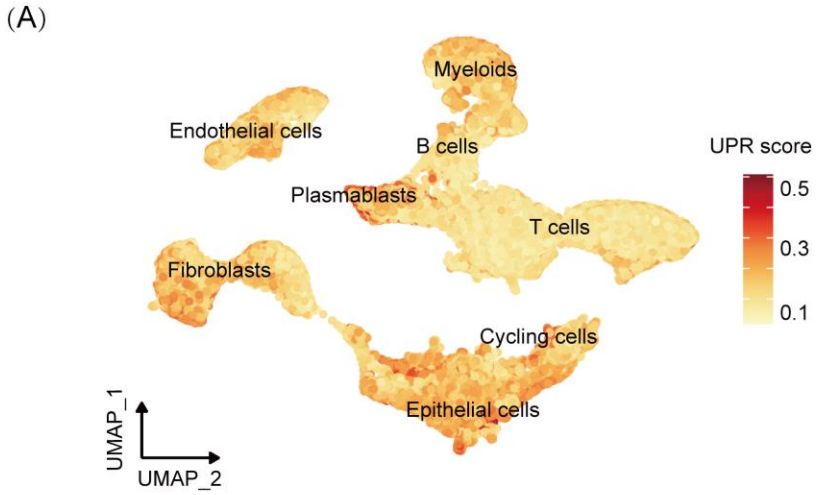


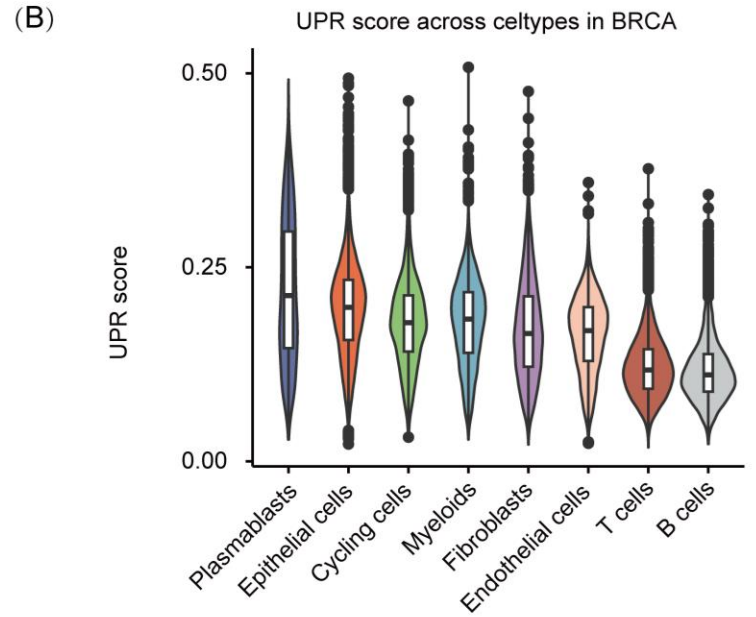


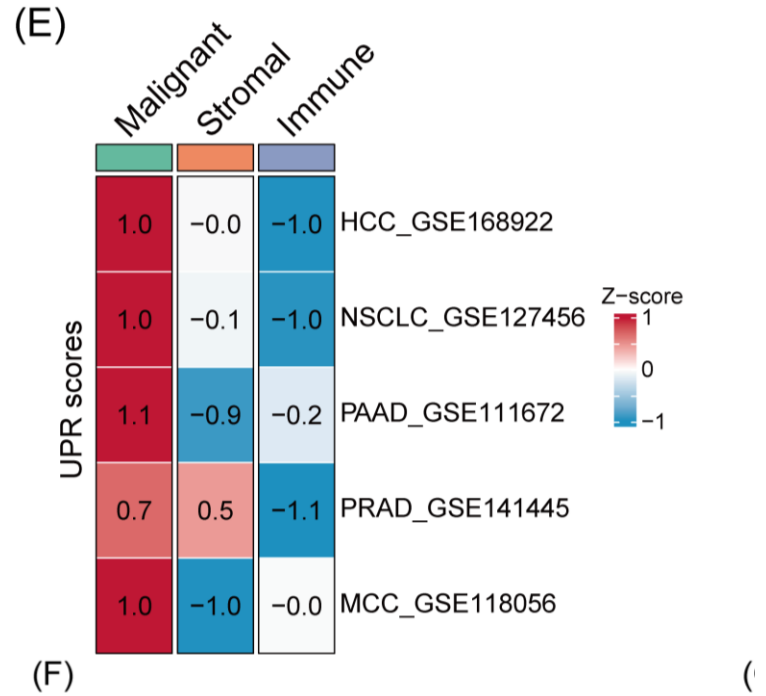
UPR activation exhibits cancer-type-specific associations with immunosuppression, tumor stemness, and other key tumor characteristics.

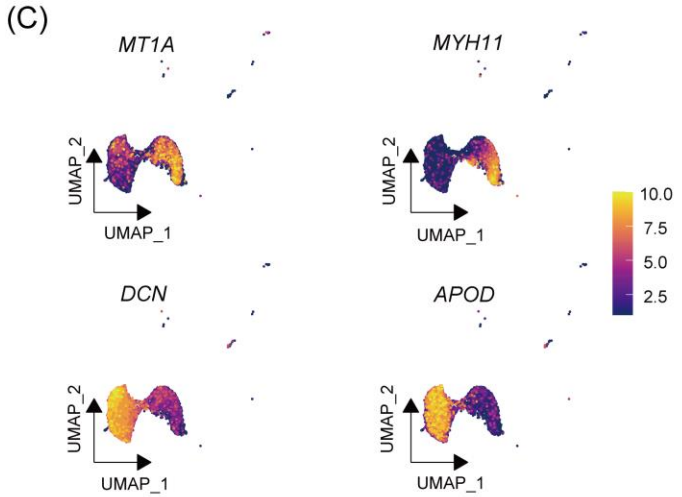
Results

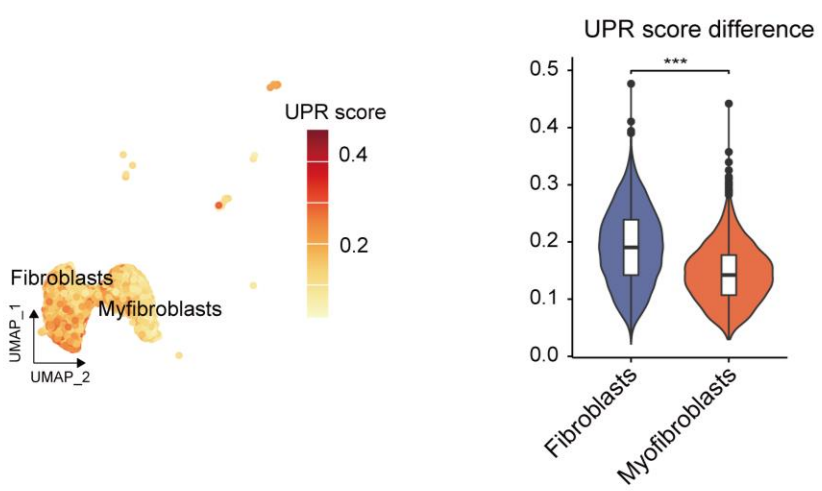
Significant intratumoral UPR heterogeneity exists, with tumor cells showing the highest UPR scores, while stromal cells and immune cells display relatively lower UPR scores.

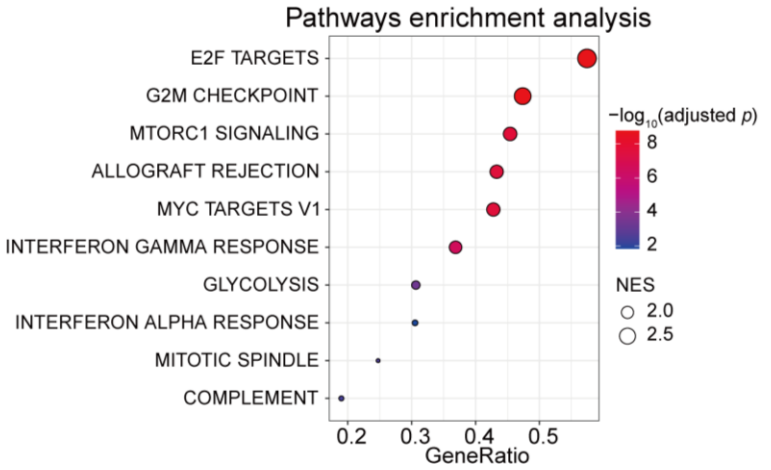






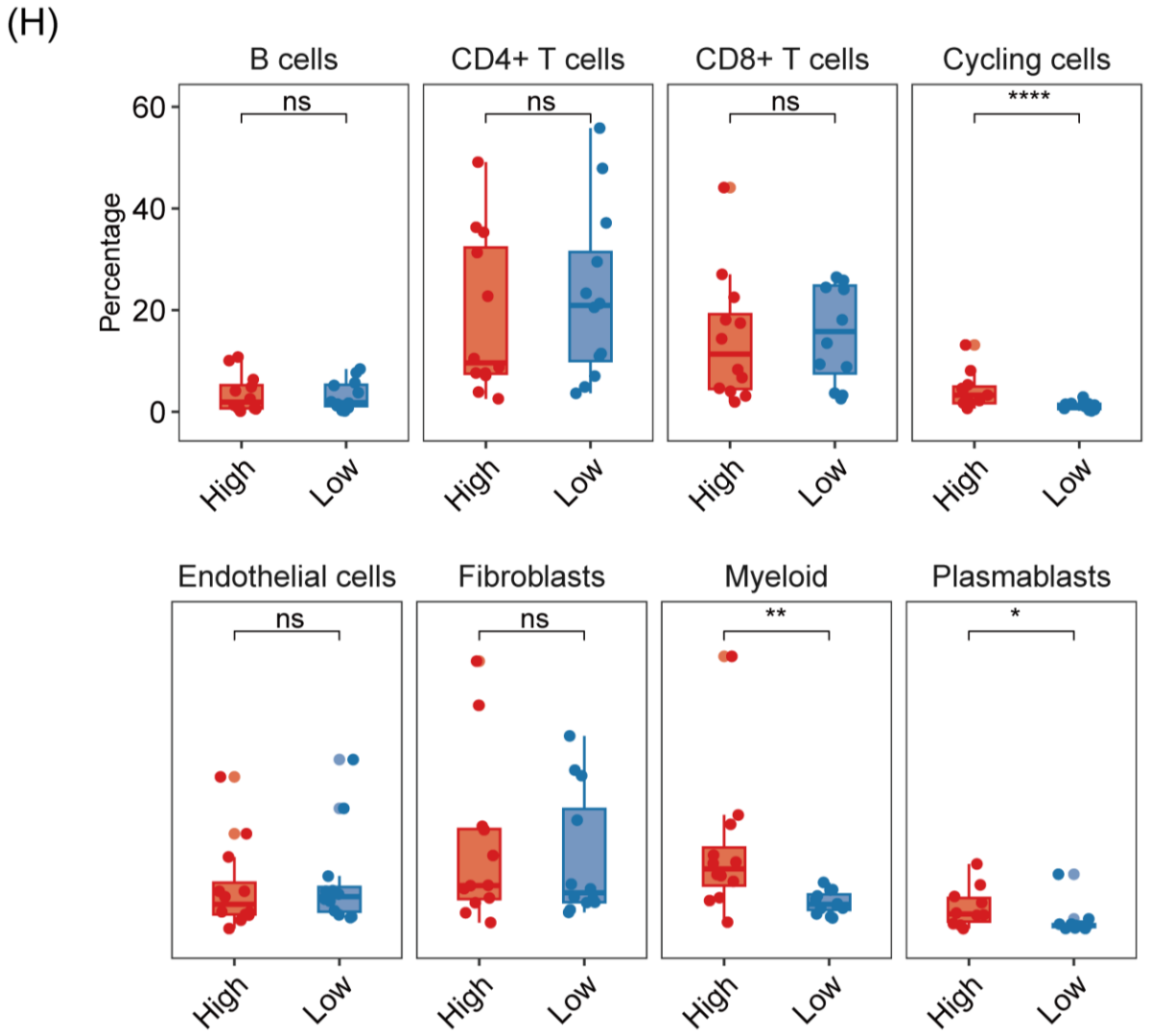


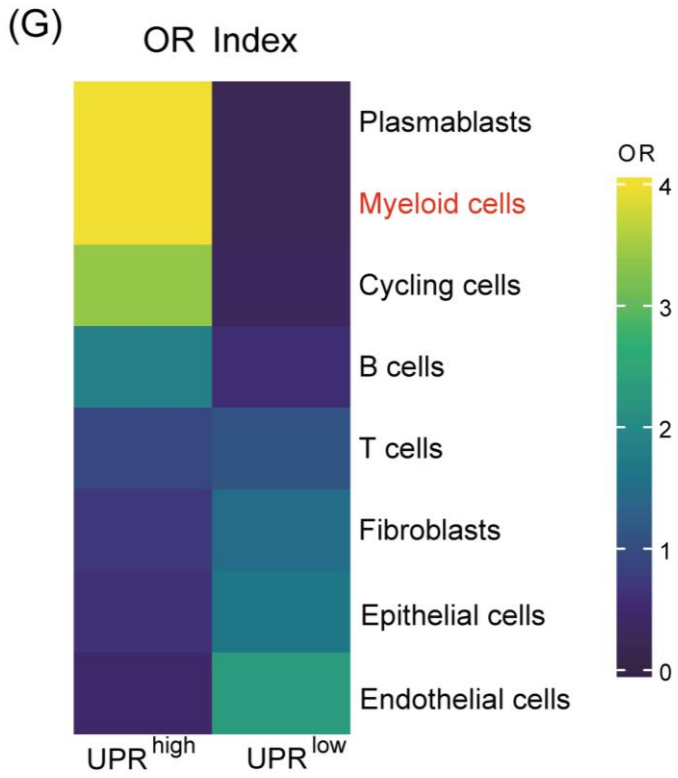




Results

Breast cancer patients with higher UPR scores are typically accompanied by increased myeloid cell infiltration.





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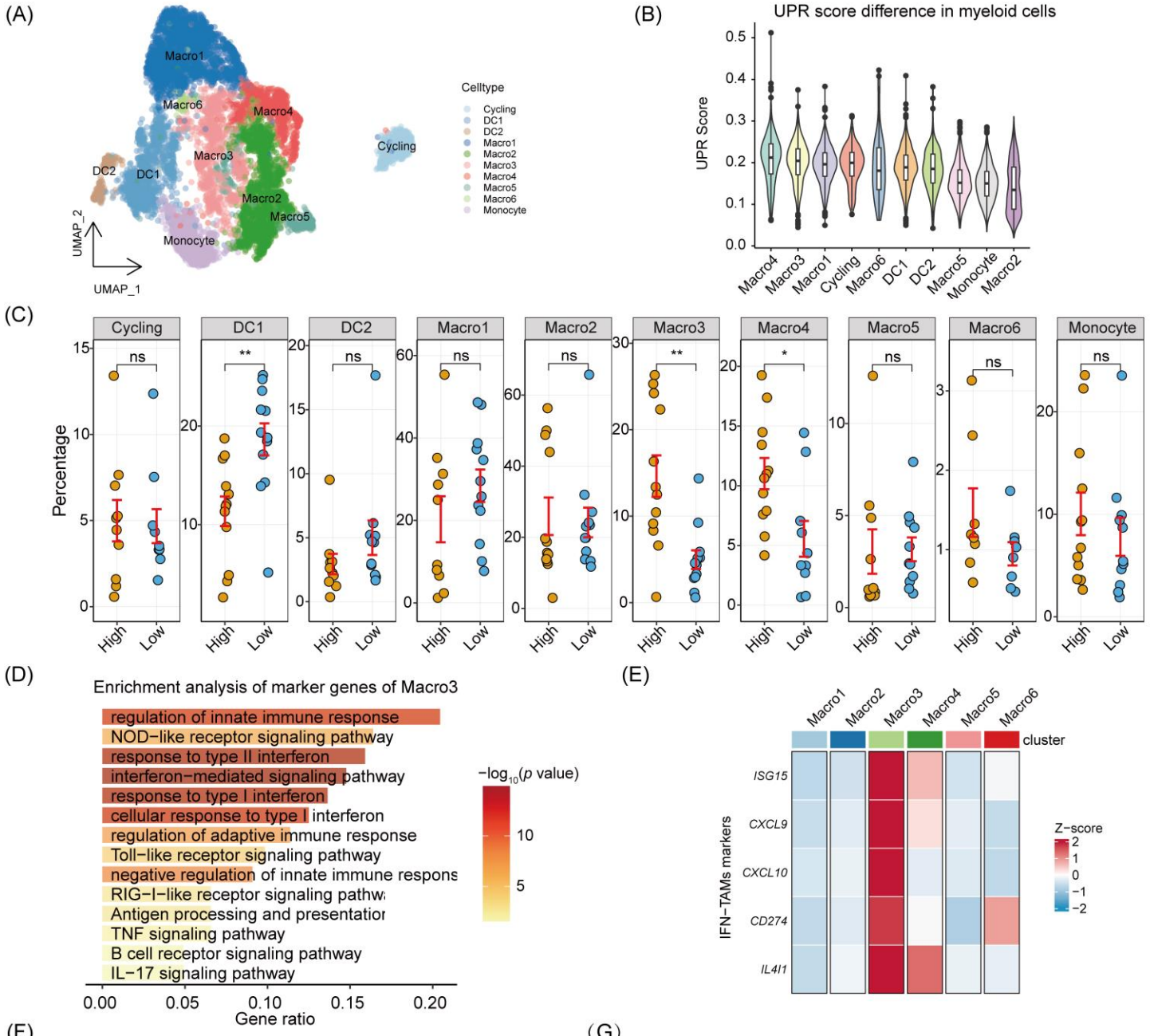
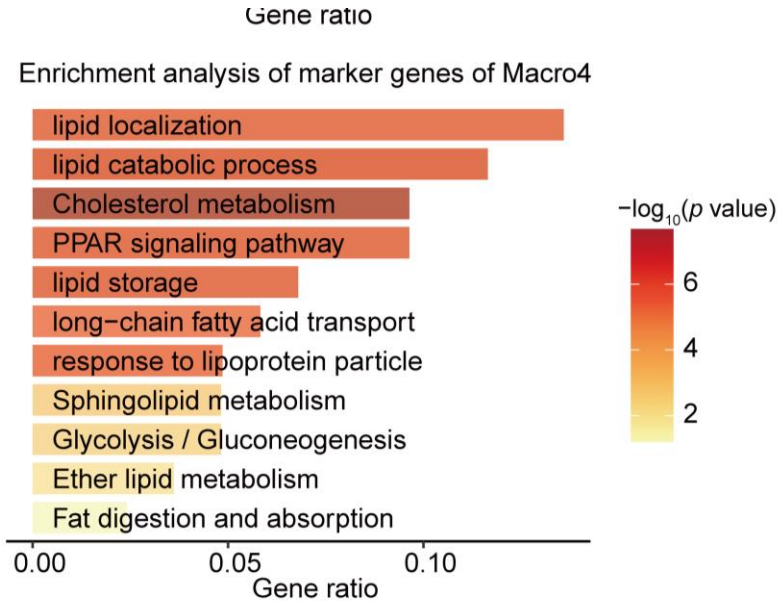


In the high-UPR group, specific myeloid cell subsets show increased infiltration within the tumor microenvironment and may promote interactions with tumor cells through the MIF signaling pathway.

Results

(F)



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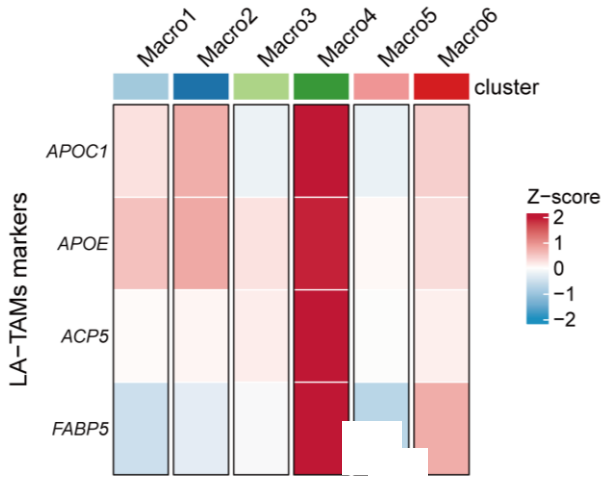

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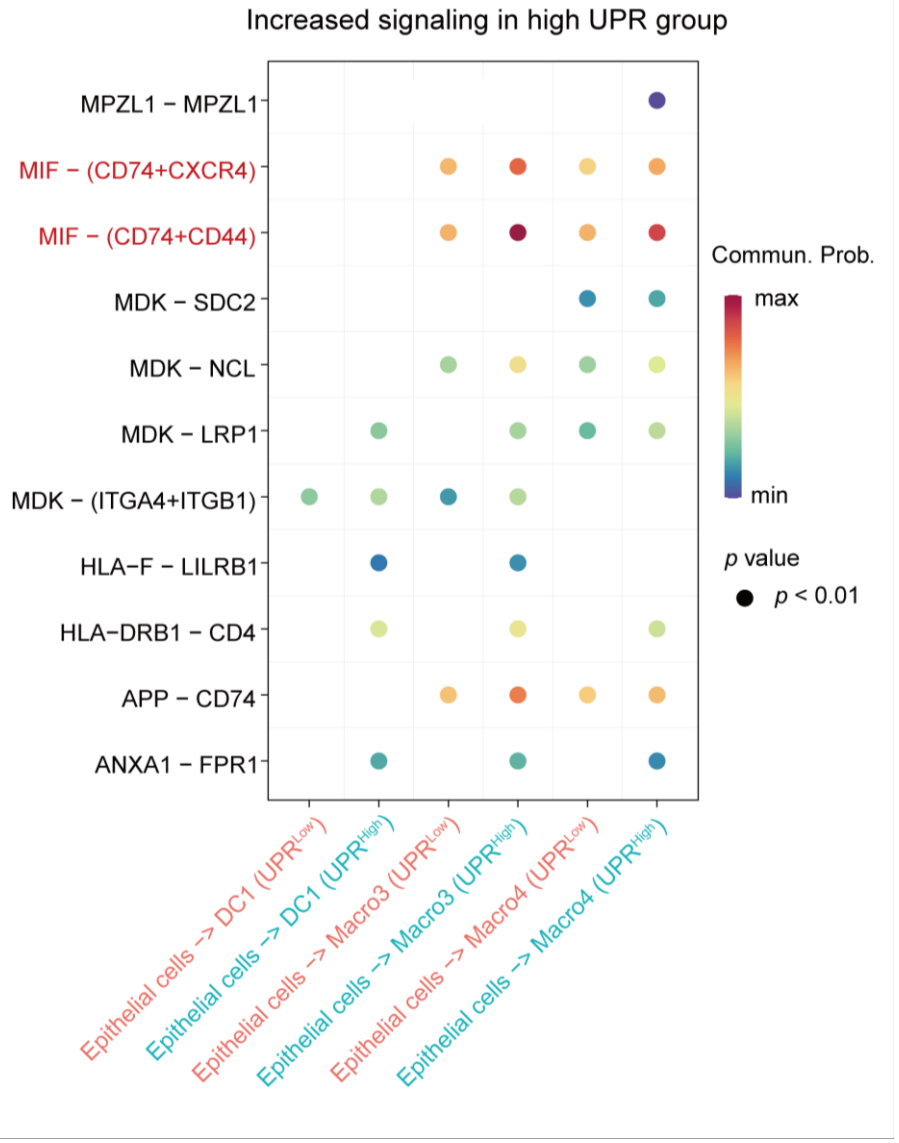
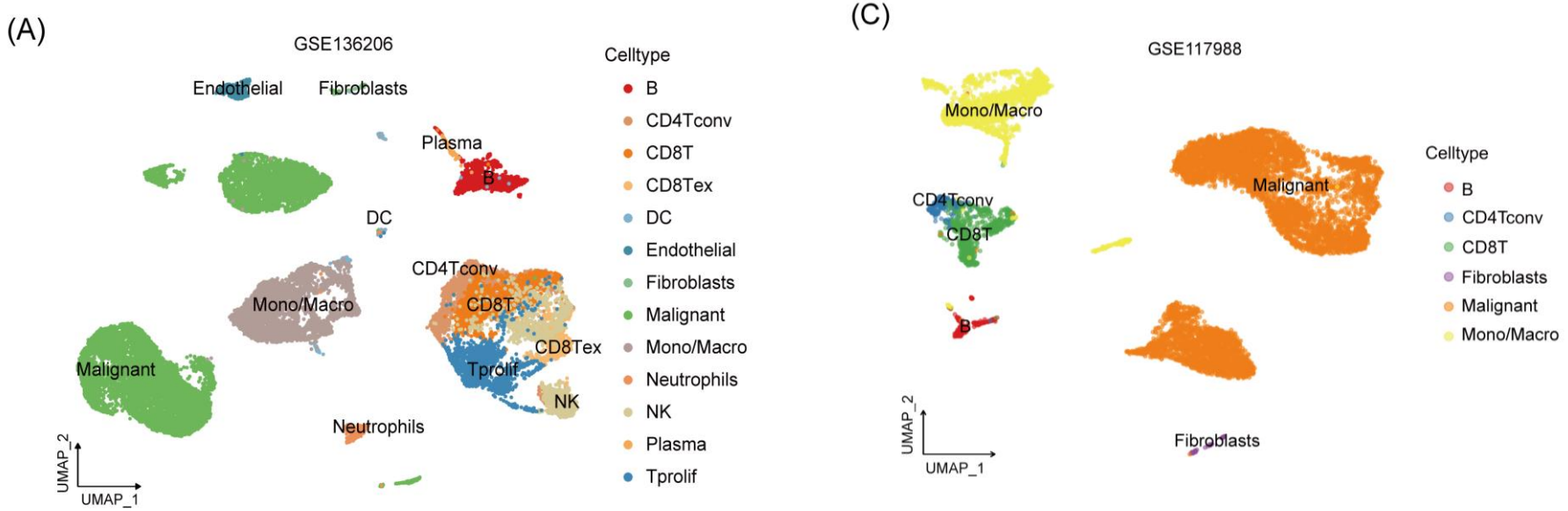
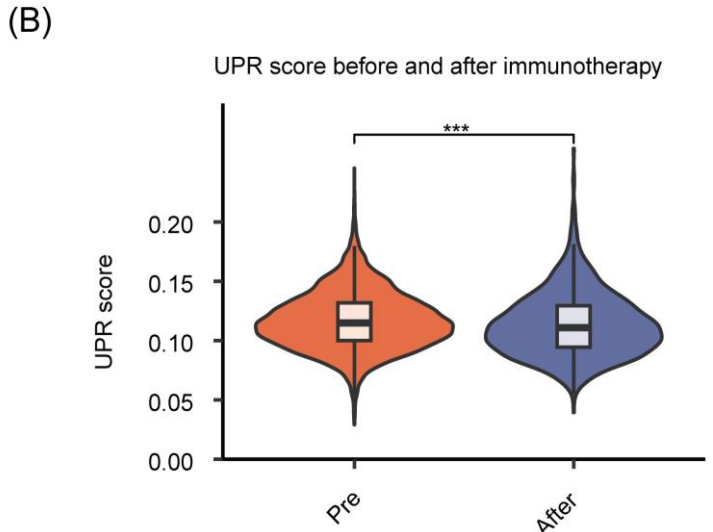


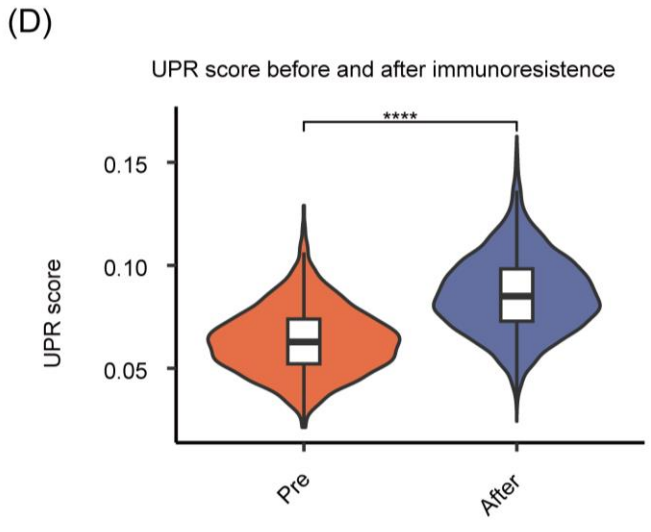
In the high-UPR group, specific myeloid cell subsets show increased infiltration within the tumor microenvironment and may promote interactions with tumor cells through the MIF signaling pathway.

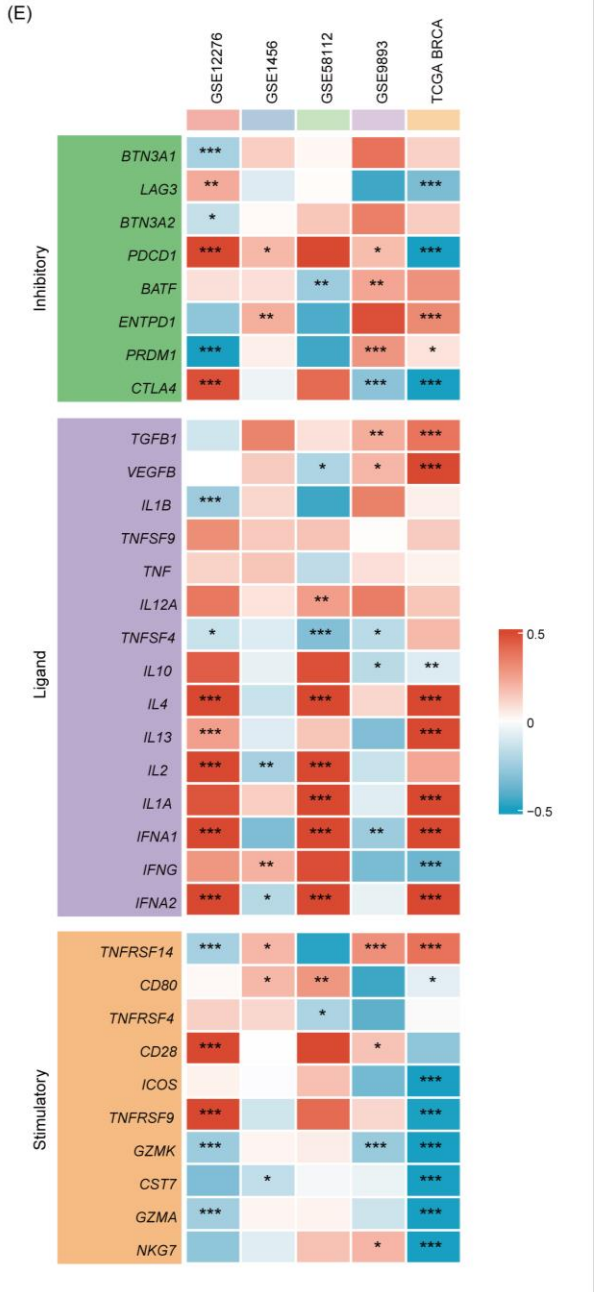
Results

Higher UPR activation is associated with impaired antitumor immune function, and tumors with elevated UPR scores may exhibit resistance to immunotherapy.









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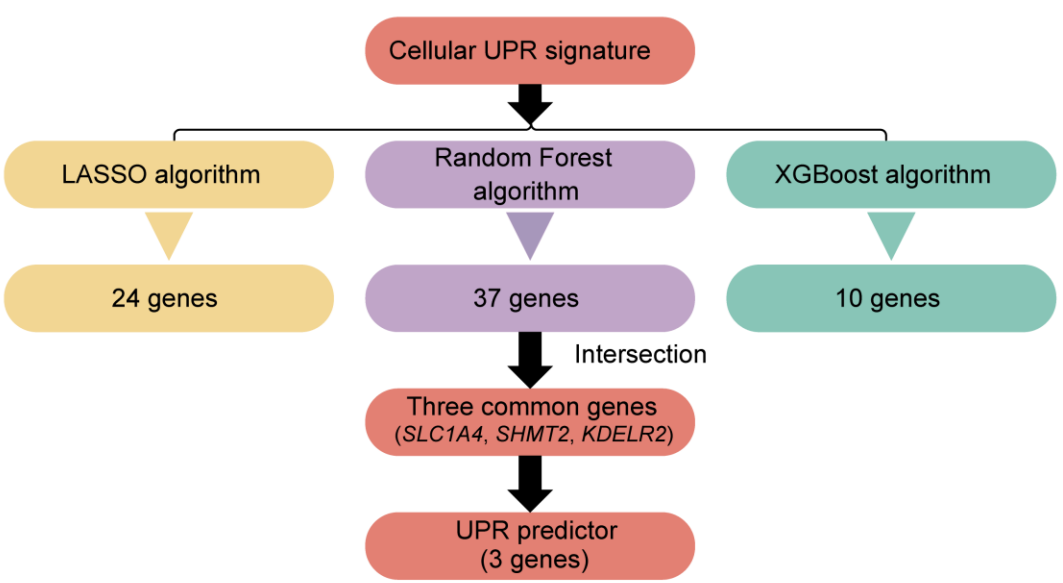
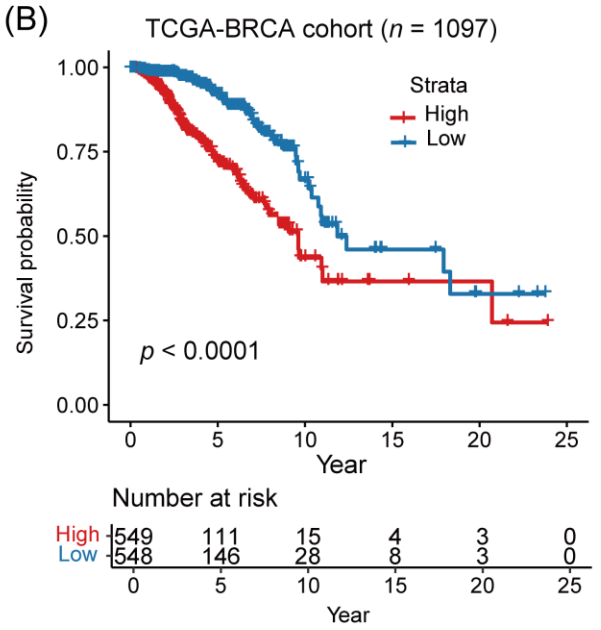
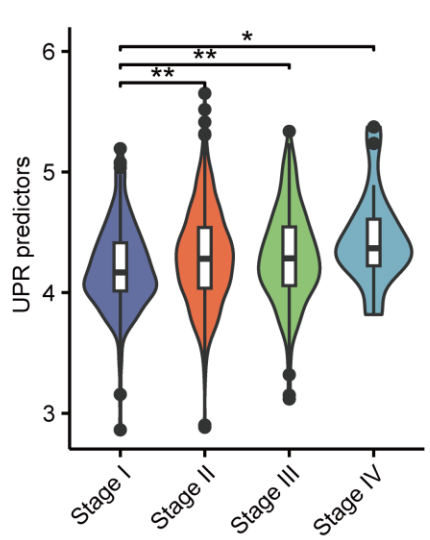
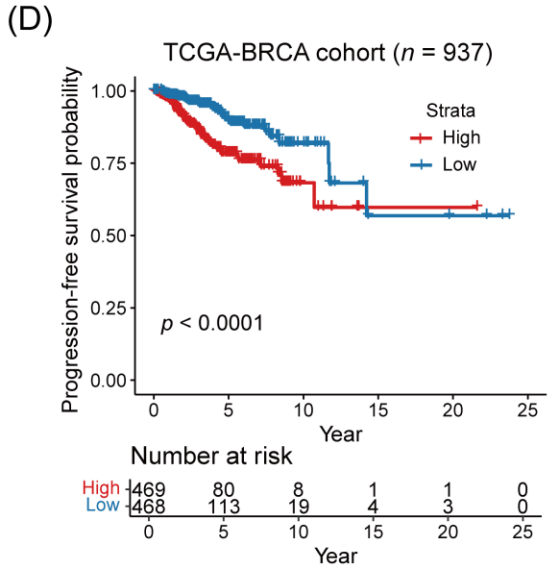
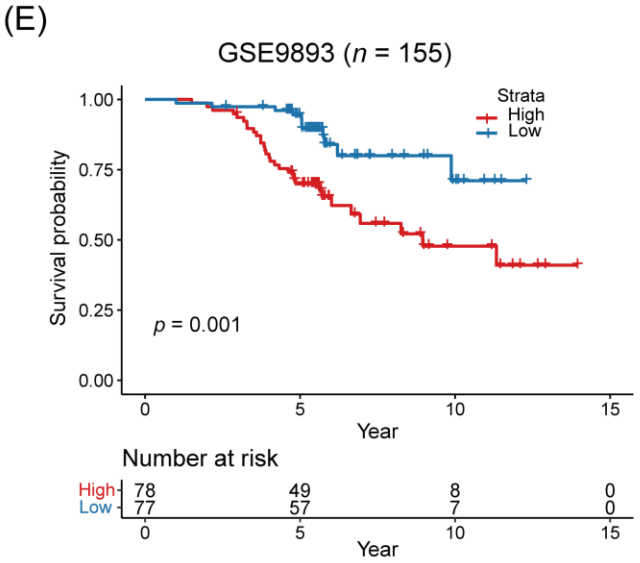




Based on UPR signature, a predictive model constructed using selected key genes effectively evaluates prognosis in breast cancer patients.







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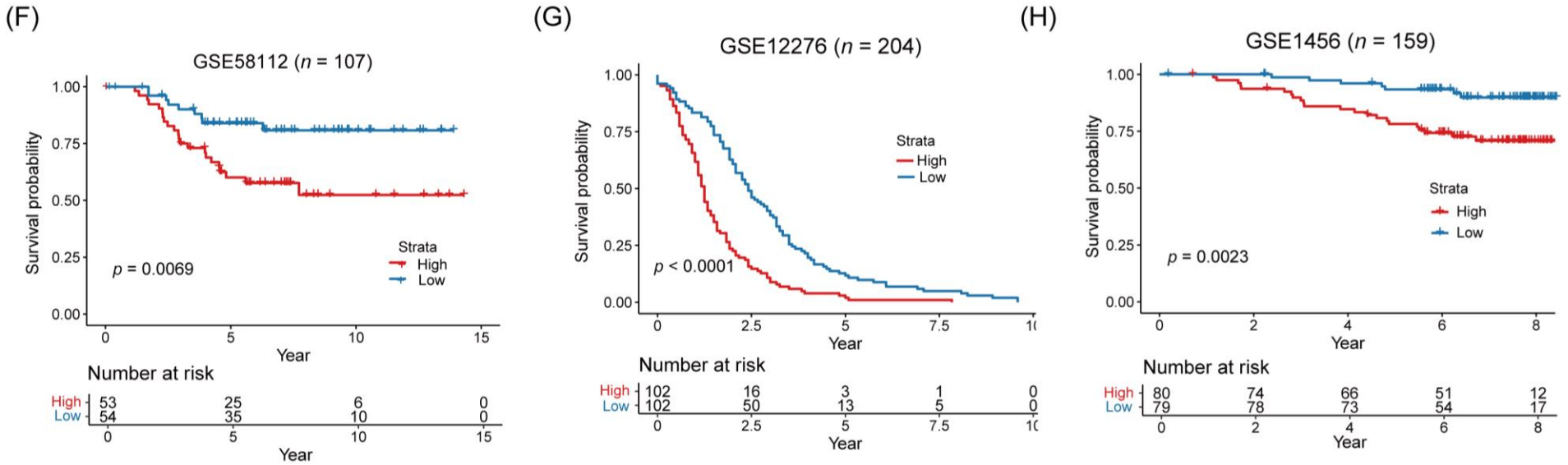

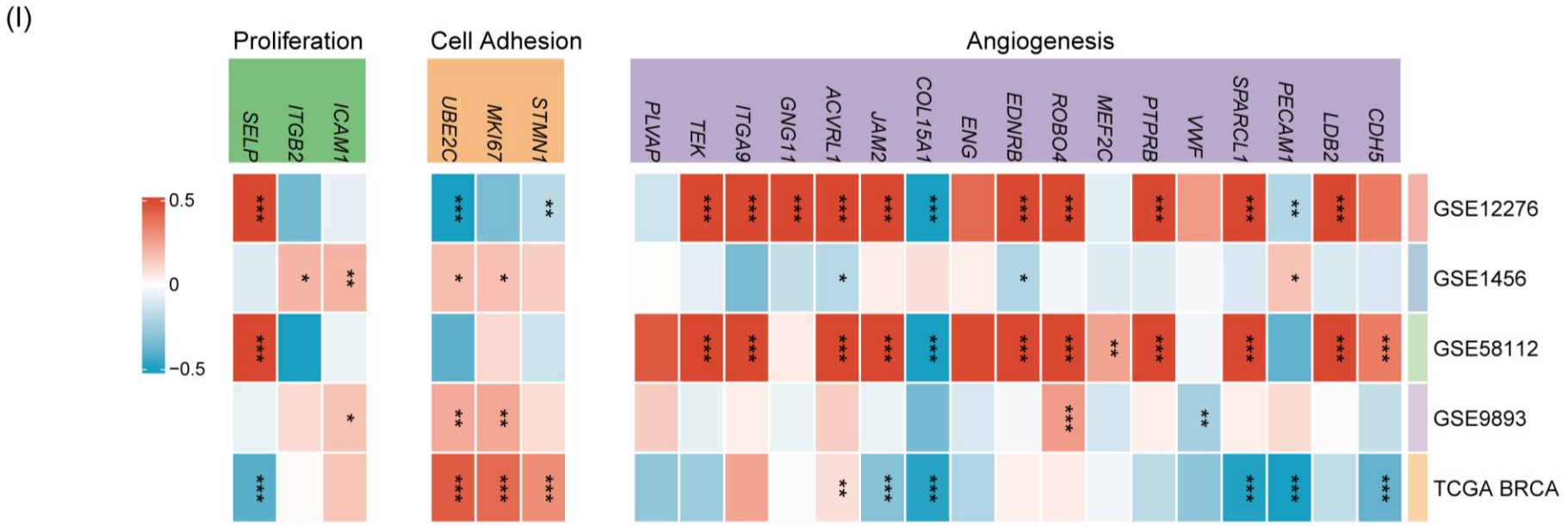

Based on UPR signature, a predictive model constructed using selected key genes effectively evaluates prognosis in breast cancer patients.

Conclusion

- In this study, we systematically evaluated UPR activity across human cancers and revealed its substantial heterogeneity across tumor types and cellular contexts, along with strong associations with key genomic and immune features.
- We also identified a UPR-related prognostic biomarker with potential clinical utility in breast cancer. Collectively, these findings deepen our understanding of the role of UPR in cancer and provide a valuable reference for future investigations into its mechanistic and therapeutic relevance.

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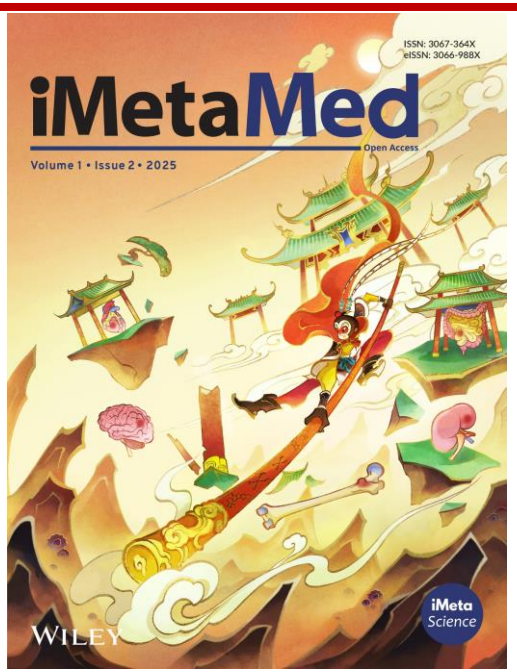

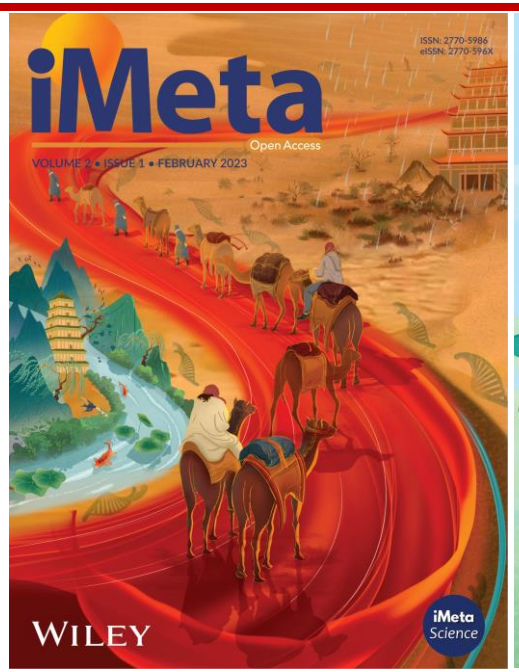

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