

Distinct YAP-TEAD Signaling States Revealed by Integrated mRNA and Protein Analysis in Thymic Epithelial Neoplasms

Lisa Elm, Nadja Gerlitz, Jens Neumann and Georgia Levidou

Department of Pathology, Paracelsus Medical University, Nuremberg

INTRODUCTION & AIM

- Thymic epithelial tumors (TETs) are biologically heterogeneous neoplasms with limited molecular stratification.
- The Hippo pathway regulates tumor progression through YAP–TEAD signaling, but the relationship between transcript levels and compartment-specific protein localization remains unclear.
- Therefore, we integrated RT-qPCR and immunohistochemistry (IHC) to identify coordinated expression and localization patterns across different TET subtypes (A, B1-B3, thymic carcinoma [TC]).

METHOD

- FFPE TET cohort: IHC (n = 77), RT-qPCR (n = 26)
- IHC: nuclear/cytoplasmic scoring of Hippo markers
- RT-qPCR: MST1, SAV1, LATS1, MOB1A, YAP1, TEAD4
- Expression normalized to HPRT1/TBP ($2^{-\Delta\Delta Cq}$)
- Spearman correlation analysis
- Principal component analysis (PCA; z-score normalization, KMO = 0.71) integrated mRNA expression with YAP1/AYAP/TEAD4 protein localization.

RESULTS & DISCUSSION

- mRNA–protein concordance was absent for upstream Hippo components but increased toward downstream YAP–TEAD effectors, with strongest coupling observed for active YAP1 (AYAP).
- PCA identified subtype-associated YAP–TEAD signaling patterns across TET entities. PC1 reflected coordinated overall pathway activity, whereas PC2 captured differences in nuclear YAP/AYAP localization. Type A thymomas showed higher PC1 values, B1/B2 lower activity profiles, B3 heterogeneous distributions, and TC distinct PC2-associated nuclear signaling patterns.

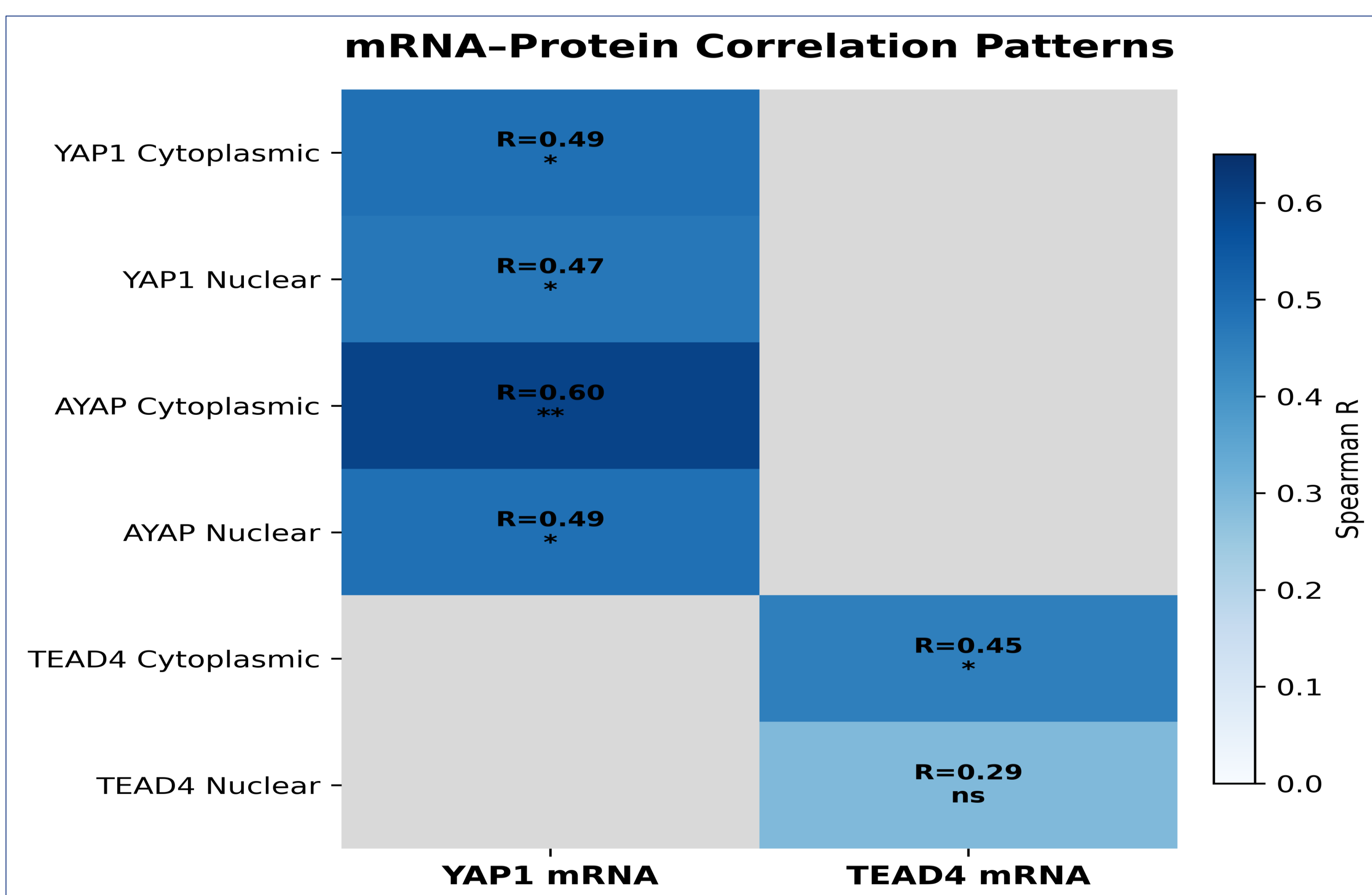


Figure 1. Heatmap of significant mRNA–protein correlations in downstream Hippo effectors.

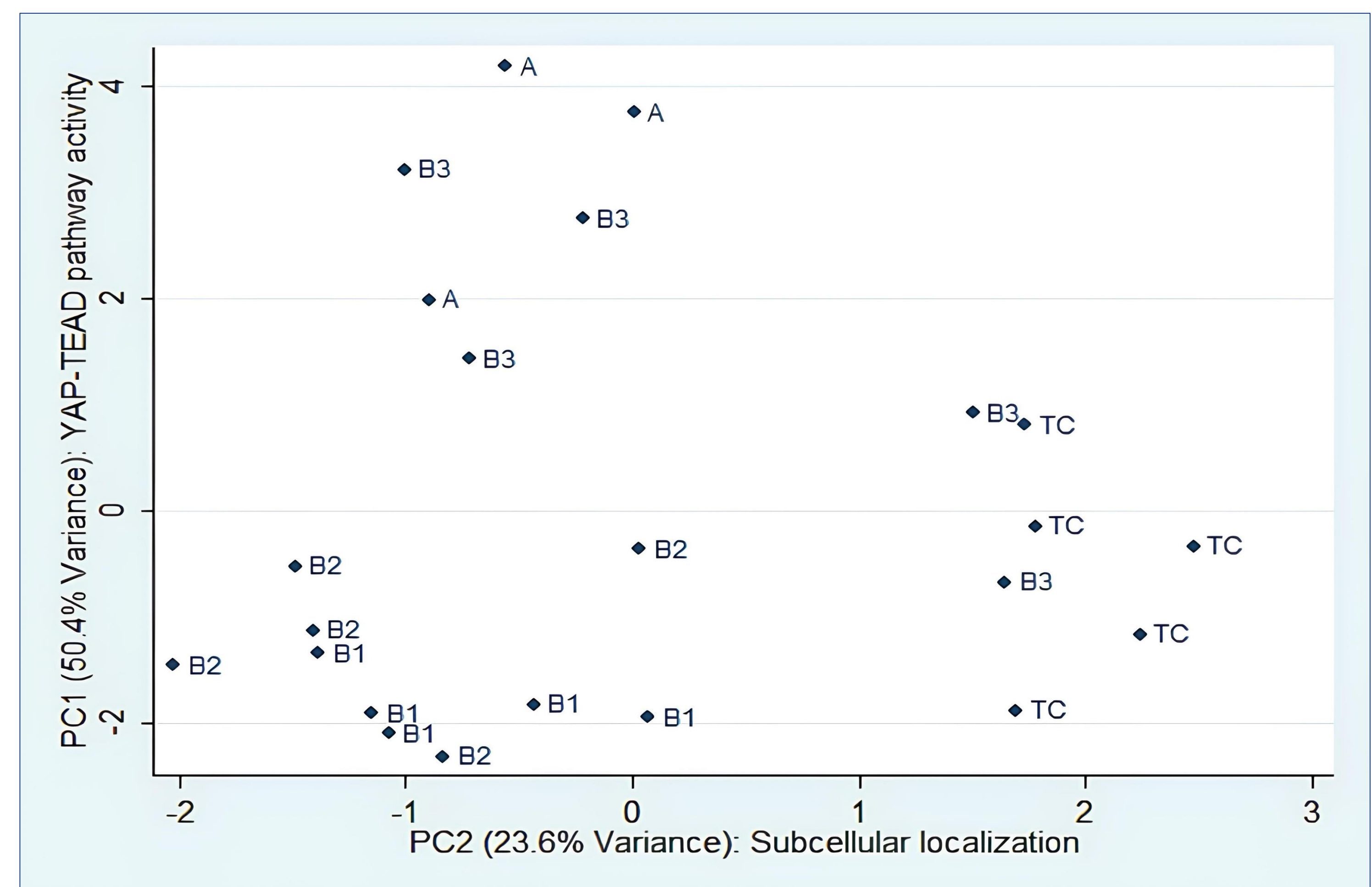


Figure 2. PCA revealing subtype-associated YAP–TEAD signaling states.

- Nuclear versus cytoplasmic compartmentalization contributed to subtype-specific signaling patterns.
- Integrative profiling may improve biological stratification of TETs beyond morphology alone.

CONCLUSIONS

Downstream Hippo effectors showed stronger transcript–protein concordance than upstream pathway components. Integrative PCA identified subtype-associated YAP–TEAD signaling states, supporting compartment-resolved molecular profiling as a complementary biomarker approach in TETs.

REFERENCES

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