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Summary

MULTI-STAGE ANALYSIS OF PANCREATIC CANCER TUMORS UNRAVELS THE ROLE OF HUMORAL IMMUNITY AS A DRIVER OF PATIENT OUTCOMES

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Multi-compartment transcriptomic classifiers incorporating tumor microenvironment immune composition improve prognostic prediction in pancreatic ductal adenocarcinoma across all disease stages.

KEY POINTS

- Unsupervised clustering of 443 pancreatic cancer transcriptomes identified four distinct immune clusters with significantly different survival outcomes, validated in two independent cohorts.
- Patients with tumors enriched in B cells and activated dendritic cells (IC1) showed the best overall survival (HR 0.57, 95% CI 0.41–0.78, P<0.001), followed by those with CD8+ T cell predominance (IC2, HR 0.70).
- The frequency of the favorable B cell and dendritic cell-enriched cluster decreased progressively from Stage I (45.7%) to Stage IV (17.1%), suggesting stage-dependent shifts in immune composition.
- Multi-compartment classifiers incorporating both tumoral cells and tumor microenvironment components outperformed classifiers based solely on tumoral cells, with the MR-Gradient model showing the best fit (HR 0.68, P<0.001).
- This work provides a framework for stratifying pancreatic cancer patients based on immunological composition of the tumor microenvironment to potentially guide personalized therapeutic approaches.

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