SPATIALLY RESOLVED DYNAMICS OF HETEROGENEOUS CANCER SUBCLUSTERS AND CANCER-ASSOCIATED NICHES IN HUMAN PANCREATIC CANCER

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Single-cell and spatial transcriptomic analysis of 17 pancreatic cancers identified five epithelial subclusters including a novel prognostic Ep_VGLL1 transitional population and six fibroblast subtypes, revealing a putative cancer progression axis and distinct tumor-proximal versus tumor-distant microenvironmental niches.

KEY POINTS

- Five distinct pancreatic cancer cell subclusters and six cancer-associated fibroblast subclusters were identified through single-cell RNA sequencing of enriched epithelial cells and fibroblasts from 17 pancreatic cancer tissues
- A novel cancer cell subcluster, Ep_VGLL1, showed intermediate characteristics between basal-like and classical subtypes with prognostic value and molecular features suggesting transitional properties
- Spatial transcriptome analysis using 10X Visium constructed an adjacency network revealing a putative cancer progression axis from Ep_FXYD2 and ADM population through Ep_TRIM54 and Ep_VGLL1 to Ep_KRT6A, supporting a model of pancreatic cancer cell dynamics
- Fb_LRRC15 myCAF populations were highly correlated with pancreatic cancer cell distributions in tumor-proximal niches, while Fb_SFRP1 iCAF populations were located distal to the cancer-associated niche
- The integrative analysis successfully deconvoluted most features from bulk transcriptome analysis and provides a comprehensive landscape suggesting potential therapeutic targets

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