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Defining Novel Ecotypes in Lymphoepithelioma-like Carcinoma of the Bladder through Spatial Transcriptomics

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Lymphoepithelioma-like carcinoma of the bladder (LELC-B) is an exceptionally rare variant of bladder cancer, predominantly categorized under the basal molecular subtype. However, a unique case of LELC-B exhibiting both luminal and basal characteristics presents an intriguing opportunity to delve deeper into the spatial and molecular landscape of this rare cancer. This study pioneers the use of spatial transcriptomics to capture the intricate gene expression heterogeneity within bladder cancer and seeks to define novel ecotypes through the spatial co-occurrence of cell types and their gene expression states.

We employed spatial transcriptomics (Visium) across three distinct bladder cancer samples: LELC-B with mixed luminal and basal features, conventional urothelial carcinoma (UC) with luminal characteristics, and conventional UC with both luminal and basal traits. Cell type deconvolution was performed to extract precise proportions and gene expression profiles at the spatial level, enabling a granular understanding of the cellular composition within each sample. Each cell type was then classified based on gene expression states, facilitating the identification of ecotypes through spatially co-occurring cell states.

we integrated these spatially-defined ecotypes with bulk RNA-seq data, leveraging deconvolution techniques to map the ecotypes back to clinical datasets. This approach allowed us to explore the clinical relevance of these ecotypes, particularly in terms of overall survival and differential drug responses. By merging cutting-edge spatial transcriptomics with bulk RNA-seq analysis, this study seeks to illuminate the complex molecular interplay within LELC-B and conventional bladder cancers, offering new insights into cancer heterogeneity and its implications for patient outcomes.