Identification of single-cell and spatial markers associated with clinically relevant pathways in high-grade serous ovarian cancer

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Abstract

High-Grade Serous Ovarian Carcinoma (HGSOC) is the most lethal subtype of ovarian cancer, accounting for 70–80% of ovarian cancer-related deaths. To gain a deeper understanding of the molecular differences between tumor and normal epithelial cells, we performed an integrated analysis using single-cell RNA sequencing (scRNA-seq) and spatial transcriptomics. Epithelial cells were classified based on gene expression profiles, utilizing CopyKat analysis to distinguish between normal and tumor cells. Differential expression analysis revealed several key genes, including *LAPTM4B*, *UBE2S*, *NENF*, *CMTM8*, and *RRP36*, which were significantly upregulated in tumor epithelial cells (Log-Fold Change > 1, $p < 0.05$). Higher expression levels of these genes were associated with poor prognosis in survival analyses. Notably, these genes exhibited significant inter-patient variability, consistently across individual datasets. We further characterized cell-cell interactions, revealing a significant enrichment of autocrine signaling pathways linked to tumor growth, metastasis, and cancer progression. Specifically, the desmosome, neuromedin U (NMU), and occludin (OCLN) autocrine signaling pathways were significantly upregulated in tumor epithelial cells compared to their normal counterparts. Overexpression of the associated genes in these pathways correlated with worse overall survival outcomes, as observed in both scRNA-seq and spatial transcriptomics data. These findings highlight the critical role of tumor-specific autocrine signaling in HGSOC progression and present potential therapeutic targets for intervention.