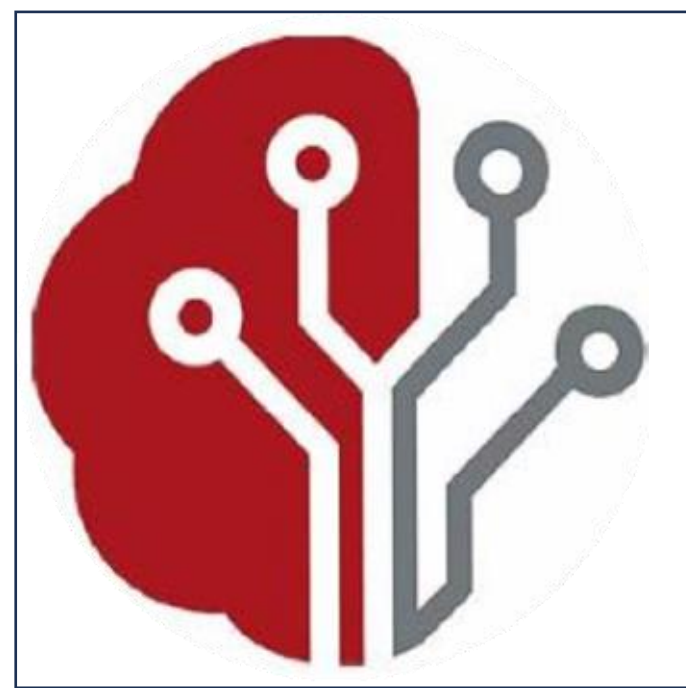




Poster # 1775: Integrative Single-Cell and Spatial Multi-Omics Reveal Tumor Heterogeneity in Lung Adenocarcinoma

Benjamin Jin¹, Qian Wang²
Correspondence: Qian Wang (qianw957@ilabri.org)



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INTRODUCTION

Lung Cancer:

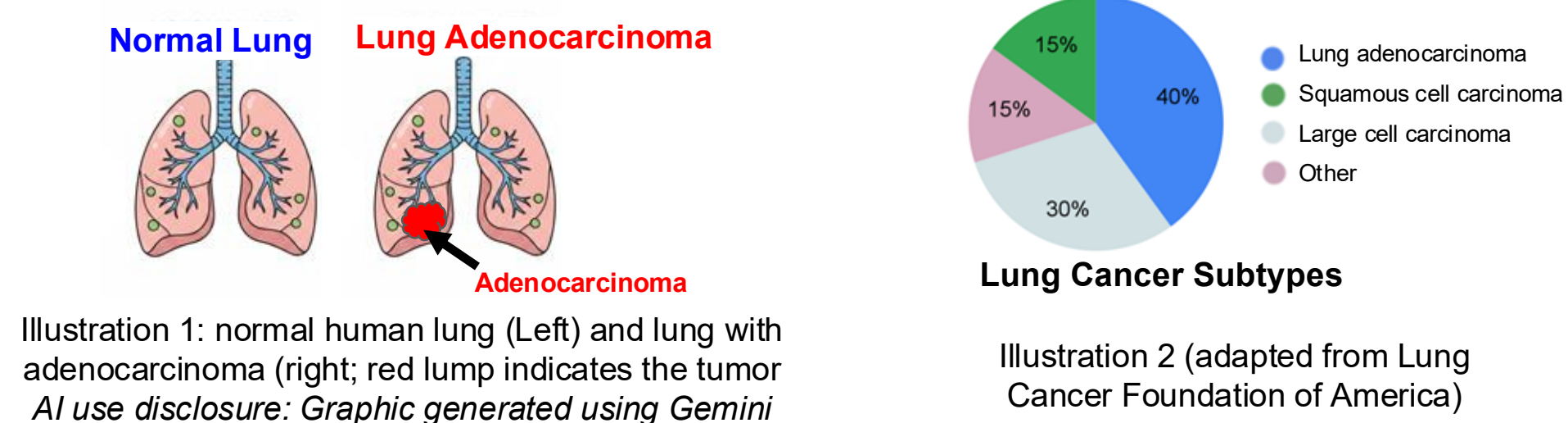
- The third most commonly diagnosed cancer in the U.S.
- remains the leading cause of cancer-related deaths worldwide
- (1.8 million deaths)

Lung Adenocarcinoma (LUAD):

- is leading type of lung cancer (~40%)
- arises from epithelial and mucin-producing cells in the outer regions of lungs

Research Gaps:

- Incomplete knowledge of tumor heterogeneity which is a key characteristic of LUAD histology.
- Gap in the understanding of underlying mechanisms of invasion and metastasis which are the main causes of death in LUAD.



METHODS

Single-Cell Transcriptomic Study (GSE198099):

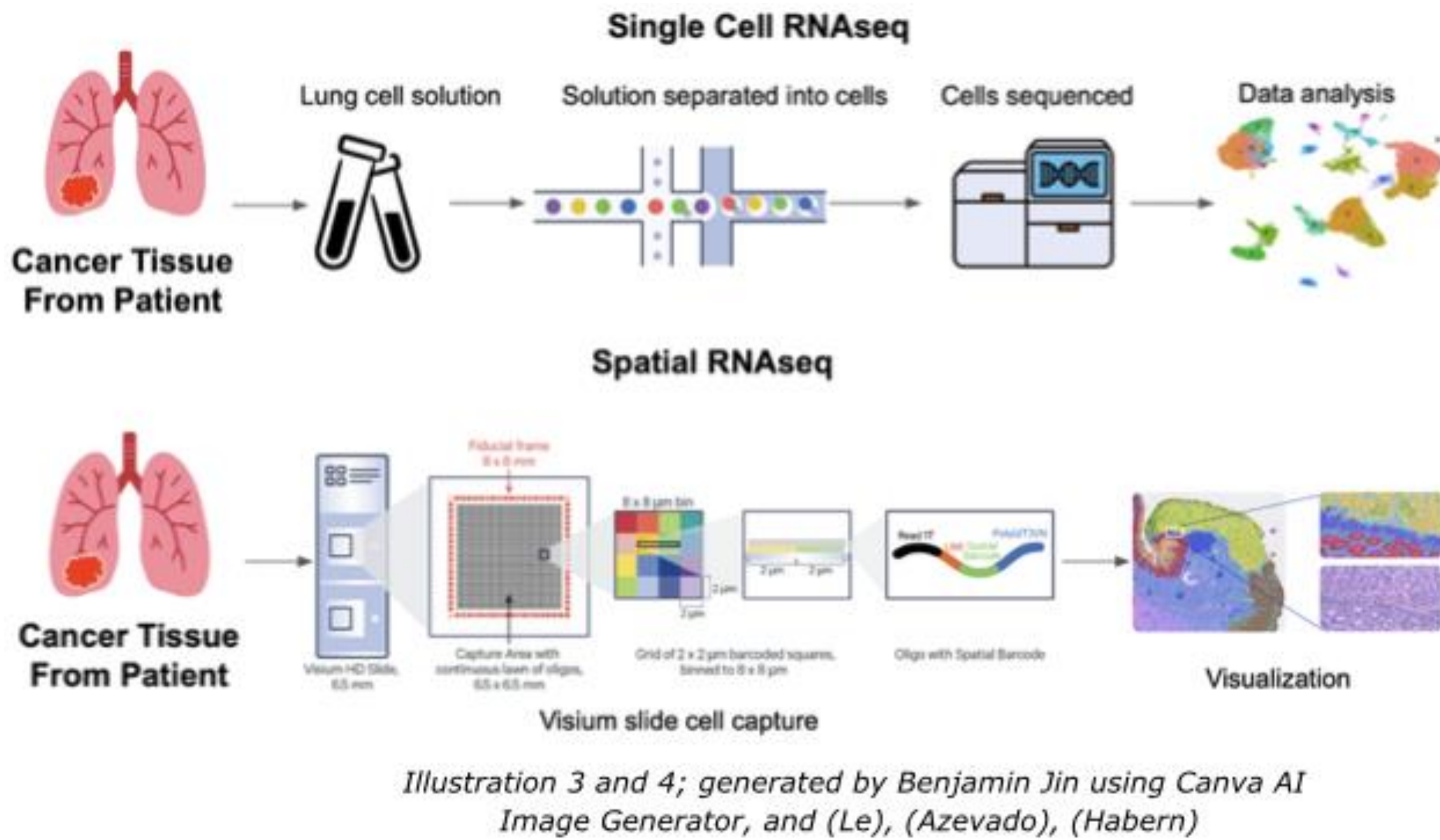
In this study, human tumor lung tissue (n=2), adjacent normal lung tissue (n=2), and adjacent lymph nodes (n=2) were studied.

Spatial Transcriptomic Study (GSE307534):

In this research, human normal lung tissue (n=1), minimally invasive adenocarcinoma (MIA, n=3) and lung adenocarcinoma (LUAD, n=3) were studied.

Immunofluorescence Histology

- Formalin-fixed paraffin embedded (FFPE) blocks of normal human lung tissue and human lung adenocarcinoma tissue sections
- Antibodies: mouse anti-human KRT7 monoclonal antibody, rabbit anti-human KRT19 monoclonal antibody, mouse anti-human MUC1 monoclonal antibody, rabbit anti-human FDPS monoclonal antibody
- Zeiss Confocal microscope



AI Use Disclosure: Gemini was used to assist in debugging R code scripts for single-cell and spatial transcriptomic data processing. All outputs and analyses were independently reviewed and validated by the authors.

DISCUSSION AND CONCLUSION

Conclusion

- Single-cell and spatial transcriptomic analyses identified three LUAD cancer cell clusters (LAC, AP-LAC, and EMT-LAC), revealing significant **intra- and inter-tumoral heterogeneity**.
- Differential gene expression patterns in tumor and adjacent tissues indicate that AP-LAC is linked to **proliferative activity**, while EMT-LAC is associated with **invasion and metastasis**.
- Spatial transcriptomic analysis confirmed that these transcriptional programs are spatially located within tumor tissues in MIA (minimally invasive adenocarcinoma) and LUAD, highlighting intra- and inter-tumoral heterogeneity and tumor evolution.
- Immunofluorescence histology confirmed specific tumor biomarkers (KRT7, MUC1, KRT19), **validating the sequencing data**

Future Research

- Establishes a framework of how canonical tumor cells evolve into specialized proliferative and invasive lineages
- Opens new avenues to investigate mechanisms driving tumor resistance, invasion, and metastatic progression.
- Provides a roadmap for investigating cell-to-cell signaling within spatial setting and evaluating the DEG markers as biomarkers for therapeutic resistance.

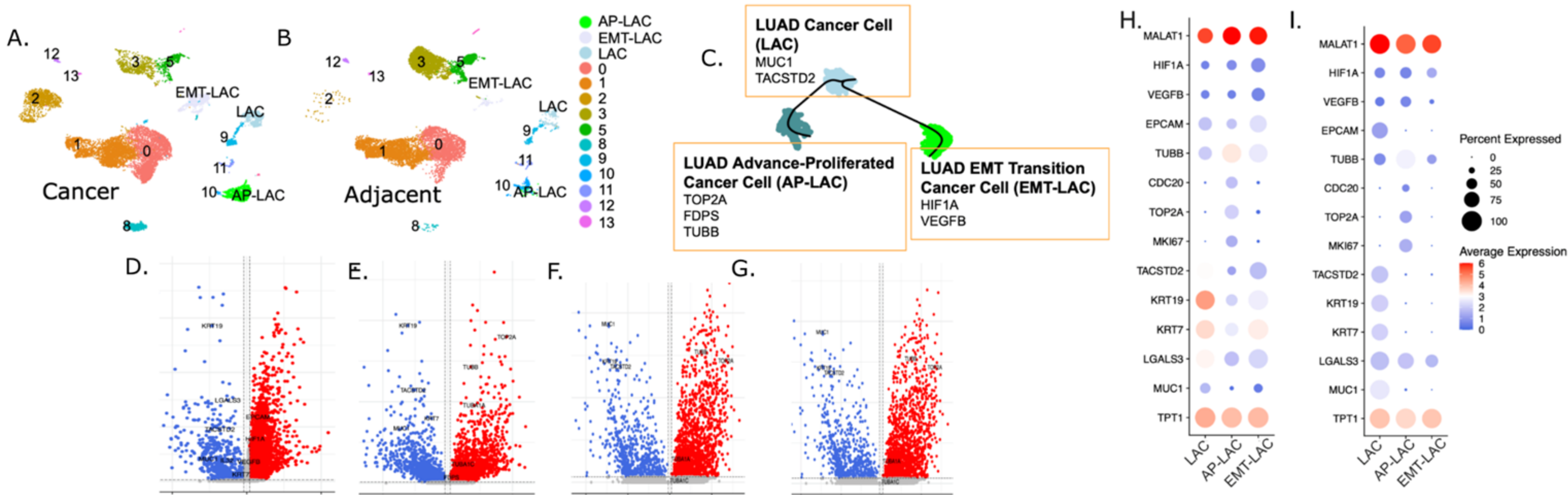
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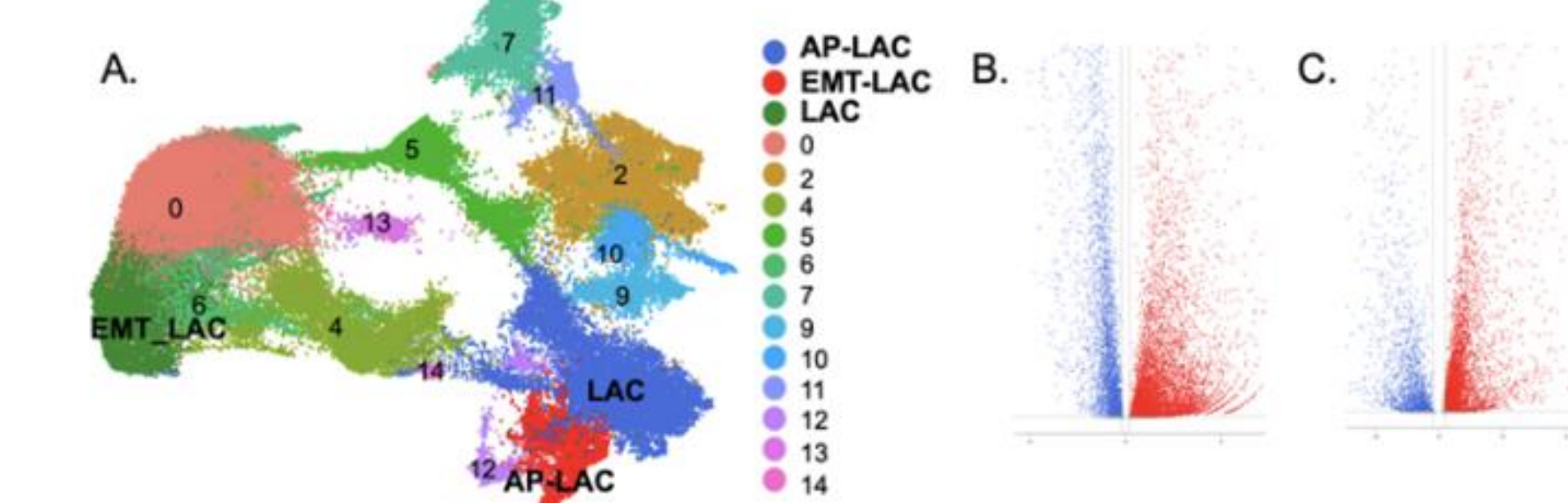
RESULTS

Result 1. Cancer Heterogeneity of LUAD: Single-cell transcriptomic analysis identified three major lung adenocarcinoma (LUAD) cancer cell clusters—LAC (LUAD cancer cells), AP-LAC (advanced proliferative LAC), and EMT-LAC (EMT-transition LAC).



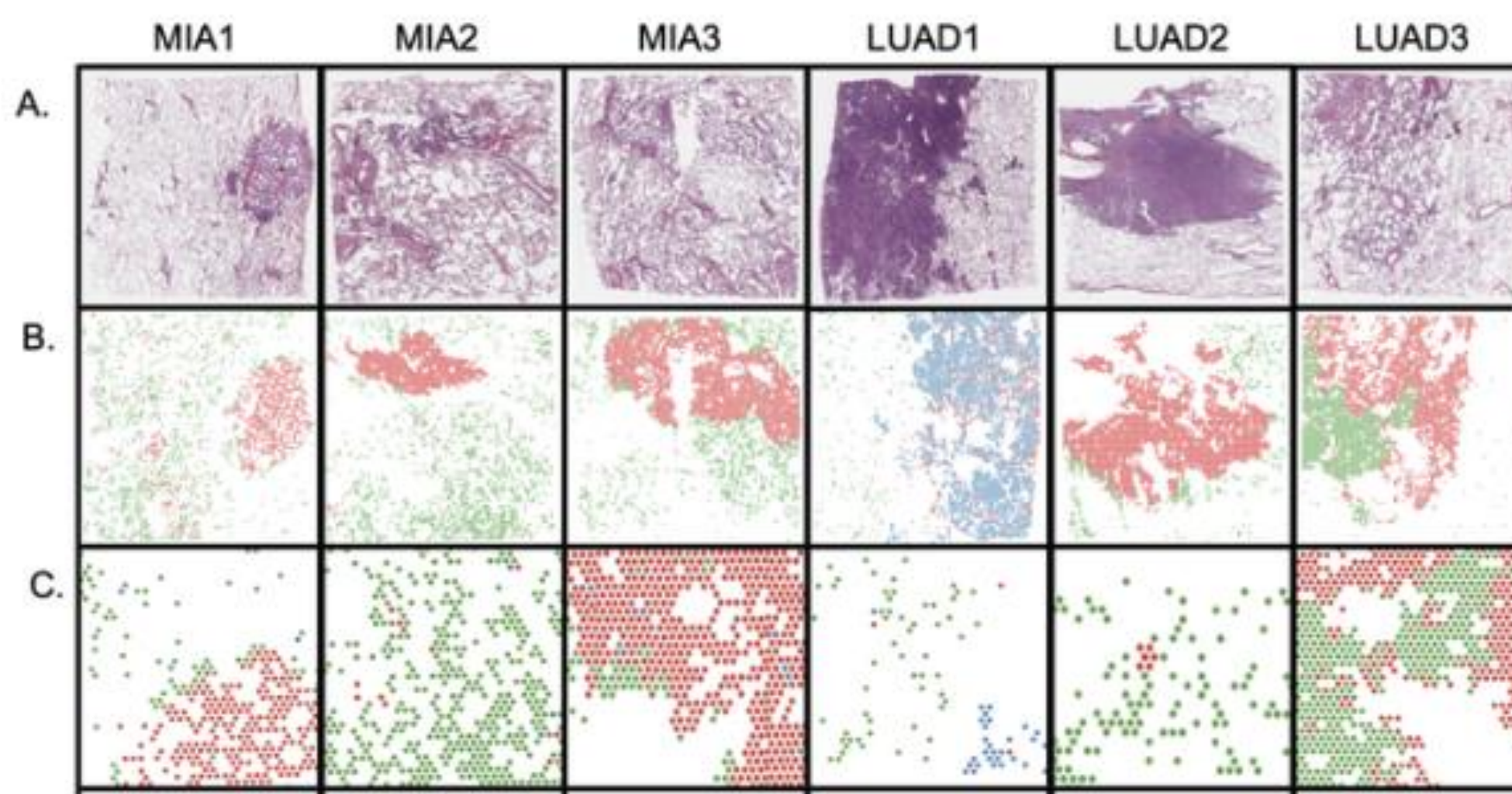
(A–B) UMAP plots of LUAD tumor tissue (A) and cancer-adjacent tissue (B), each showing three distinct cancer cell clusters and indicating tumor heterogeneity. (C) Two trajectories of cancer cell development: LAC to AP-LAC (left), representing a transition toward an advanced proliferative state, and LAC to EMT-LAC (right), representing progression toward invasive and metastatic phenotypes. (D–G) Volcano plots showing differentially expressed genes (DEGs) in EMT-LAC compared with LAC in tumor tissue (D–E) and cancer-adjacent tissue (F–G), highlighting genes associated with LUAD cell invasion and metastasis. (H–I) Dot plots showing character genes across the three clusters in cancer (H) and cancer-adjacent (I).

Result 2. Three Major Cancer Cell Clusters in MIA and LUAD Tumor Tissues.



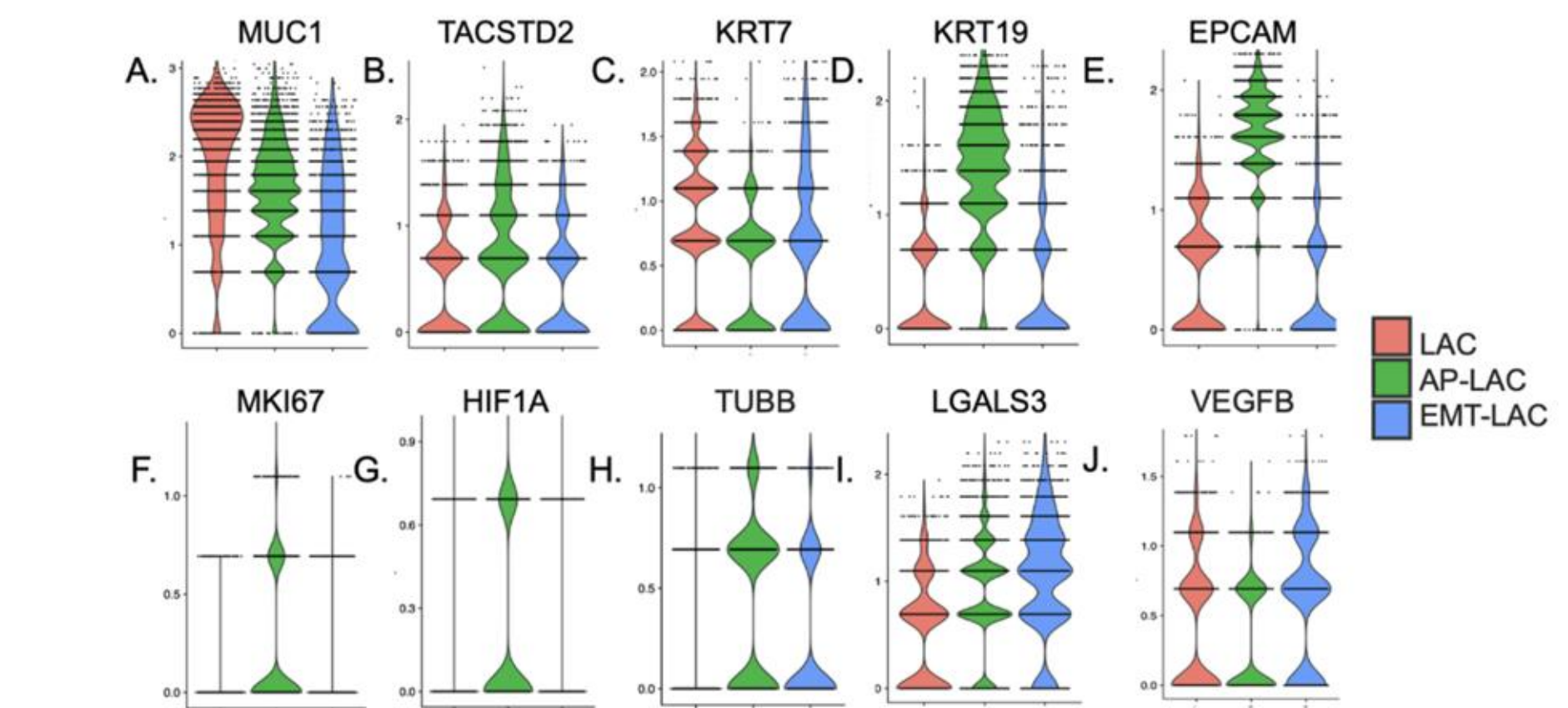
(A) UMAP of spatial transcriptomic data from normal lung, minimally invasive adenocarcinoma (MIA), and lung adenocarcinoma (LUAD) slides. Three cancer cell clusters—LAC, AP-LAC, and EMT-LAC—were identified, consistent with the scRNA-seq results. (B–C) Volcano plot showing differentially expressed genes (DEGs) in the comparison between LAC and EMT-LAC clusters (B) and LAC and AP-LAC (C).

Result 4. Spatial Distribution of LAC, Advanced AP-LAC, and Invasive EMT-LAC in MIA and LUAD Tumor Tissues.



(A) H&E images of tumor and cancer-adjacent tissues. (B) Spatial transcriptomic maps showing three cancer cell clusters LAC (red), AP-LAC (blue) and EMT-LAC (green). (C) Zoomed-in images from B highlighting EMT-LAC cells with LAC cells scattered among the EMT-LAC cells in the cancer-adjacent tissue.

Result 3. Expression of Tumor Genes Across Clusters in MIA and LUAD Tissues.



(A–J) Violin plots showing the expression of cancer biomarker genes across three cancer clusters from spatial transcriptomic analysis.

Result 5. Tumor Markers MUC1, KRT7 and KRT19 in LUAD Tumor Tissue.

