

# Characterizing Cellular Heterogeneity and Spatial Organization in Lung Adenocarcinoma with Visium HD

Sameen Hossain<sup>1</sup> and Dr. Katarzyna M. Tyc<sup>2,3</sup>

<sup>1</sup>College of Humanities and Sciences, School of Life Sciences and Sustainability, Virginia Commonwealth University

<sup>2</sup>Department of Biostatistics, School of Public Health, Virginia Commonwealth University, <sup>3</sup>Massey Bioinformatics Shared Resource Core

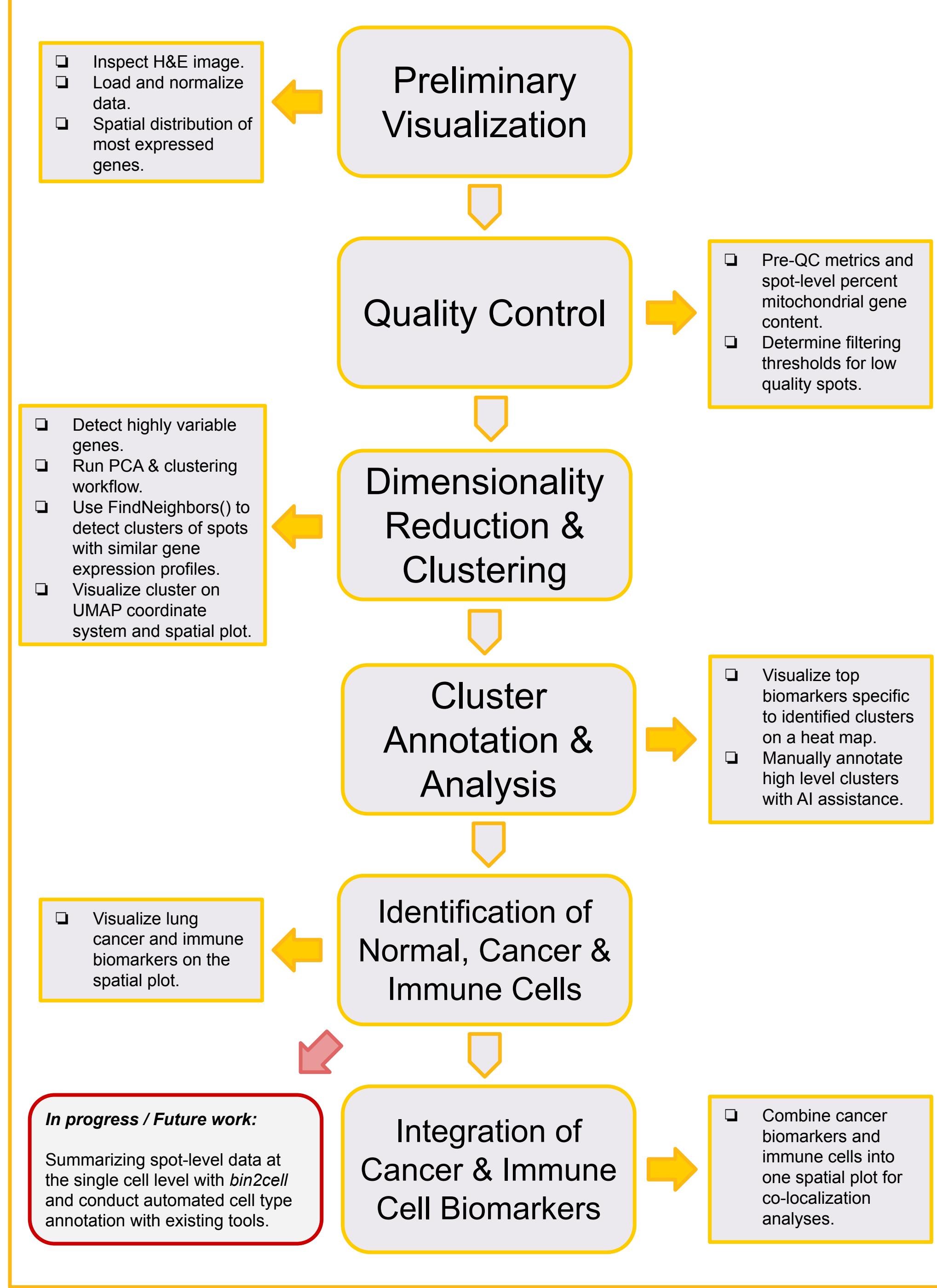
## Introduction

Spatial transcriptomics is an emerging technology that enables the profiling of gene expression while preserving the spatial context of cells within intact tissue sections. This approach offers unprecedented insights into tissue architecture and cellular neighborhoods, which are critical for understanding disease mechanisms and identifying clinically relevant biomarkers.

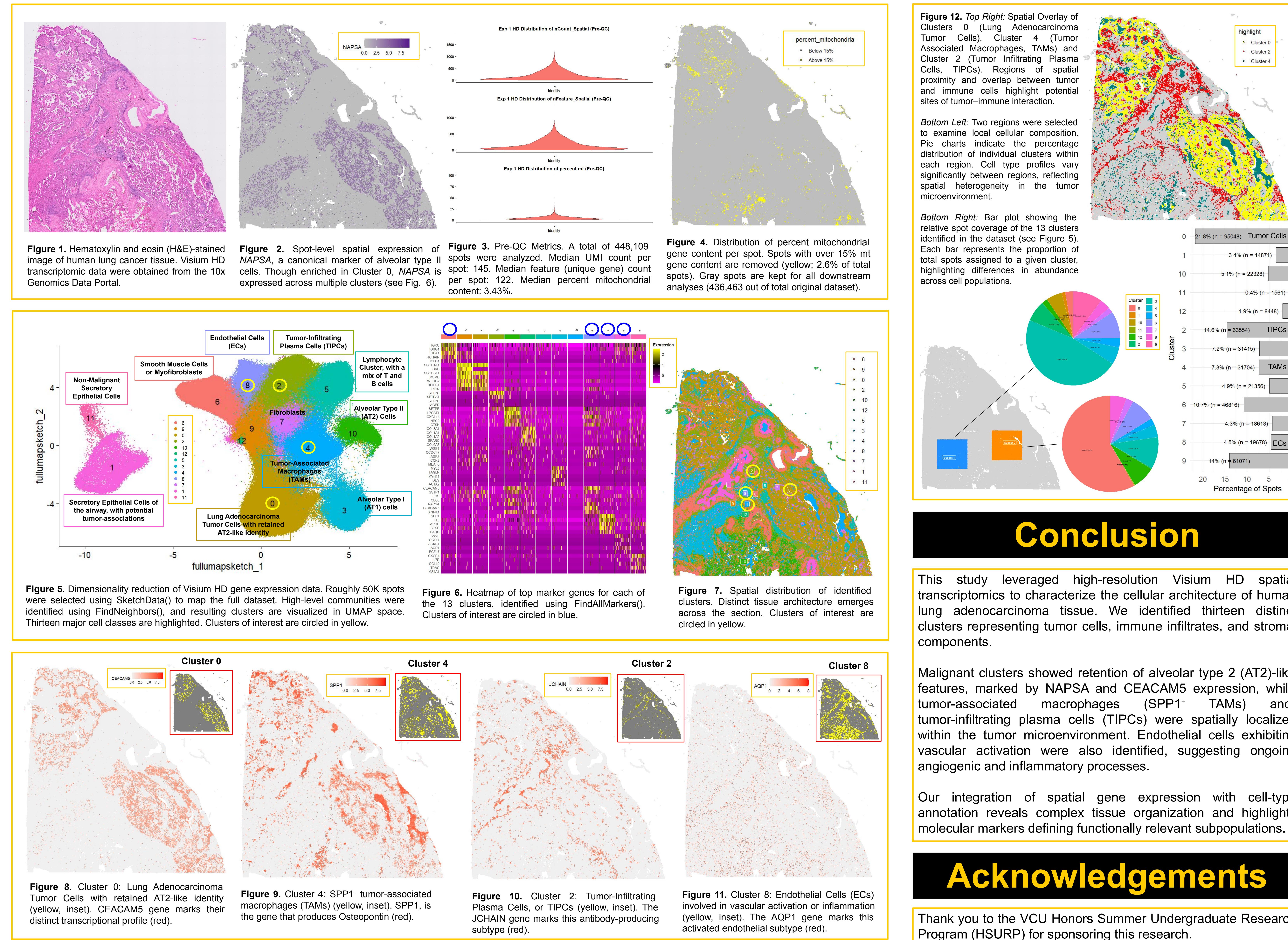
Visium HD, the latest high-resolution spatial transcriptomics platform developed by 10x Genomics, allows for detailed transcriptomic mapping across diverse tissue types. Analyzing such data requires robust computational tools. Seurat, an R package originally developed by the Satija Lab for single-cell RNA-seq analysis, has been adapted to handle spatial data, including Visium HD. Best practices in spatial transcriptomics include quality control, normalization, dimensionality reduction, and clustering—tasks supported by a growing suite of analytical tools.

In this study, we establish a streamlined, best-practice workflow for analyzing high-resolution Visium HD data using the Seurat framework. We apply this pipeline to a human lung adenocarcinoma dataset, the most prevalent form of non-small cell lung cancer (NSCLC) in the United States. Our goal is to map tumor and immune cell populations within the tumor microenvironment and highlight the utility of spatial methods for cancer research and precision medicine.

## Methodology



## Results



## Future Directions

Further analysis of cell-cell communication will enhance understanding of tumor-immune crosstalk and therapeutic targets. We plan to apply single-cell segmentation for precise biomarker mapping and study immune cell topography alongside copy number alteration (CNA)-defined tumor subclones. These efforts aim to clarify the roles of TAMs and TIPCs in lung adenocarcinoma progression and support development of targeted therapies.

## Conclusion

This study leveraged high-resolution Visium HD spatial transcriptomics to characterize the cellular architecture of human lung adenocarcinoma tissue. We identified thirteen distinct clusters representing tumor cells, immune infiltrates, and stromal components.

Malignant clusters showed retention of alveolar type 2 (AT2)-like features, marked by NAPSA and CEACAM5 expression, while tumor-associated macrophages (SPP1<sup>+</sup> TAMs) and tumor-infiltrating plasma cells (TIPCs) were spatially localized within the tumor microenvironment. Endothelial cells exhibiting vascular activation were also identified, suggesting ongoing angiogenic and inflammatory processes.

Our integration of spatial gene expression with cell-type annotation reveals complex tissue organization and highlights molecular markers defining functionally relevant subpopulations.

## Acknowledgements

Thank you to the VCU Honors Summer Undergraduate Research Program (HSURP) for sponsoring this research.

## References

Satija Lab. (2024). Analysis, visualization, and integration of Visium HD spatial datasets with Seurat. [https://satijalab.org/seurat/articles/visiumhd\\_analysis\\_vignette](https://satijalab.org/seurat/articles/visiumhd_analysis_vignette)