



P3.079: Impact of Smoking on Tumor Microenvironment of T Cells Revealed by Single-Cell RNA Sequencing

Yong Jun Choi¹, Chi Young Kim¹, Eun Young Kim², Sang Hoon Lee², Min Kyung Park¹, Yoon Soo Chang¹

¹Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea

²Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea

Correspondence: Yoon Soo Chang (YSCHANG@yuhs.ac)



IASLC 2026 World
Conference on Lung Cancer
SEPTEMBER 12 - 15, 2026
SEOUL, REPUBLIC OF KOREA

INTRODUCTION

Smoking history has been associated with improved responses to immune checkpoint inhibitor (ICI) therapy in lung cancer, suggesting that smoking-related alterations in the tumor immune microenvironment may influence antitumor immunity. However, the cellular and molecular features underlying these differences remain incompletely understood. In this study, we investigated smoking-associated changes in the tumor microenvironment of lung adenocarcinoma (LUAD) and sought to identify cellular populations and biomarkers associated with tertiary lymphoid structure formation.

METHODS

Single-cell RNA-sequencing (scRNA-seq) datasets from tumors and matched adjacent normal tissues of five current smokers and five never-smokers with LUAD were integrated to characterize smoking-associated alterations in the tumor microenvironment, with detailed analysis of the T- and NK-cell compartments [1]. Smoking-related differences in cellular composition and transcriptional profiles were assessed, and key findings were further evaluated using independent public LUAD scRNA-seq datasets [2, 3] and external bulk RNA-seq cohorts [4]. Selected cellular and spatial findings were subsequently validated by multiplex immunofluorescence in formalin-fixed, paraffin-embedded LUAD tissues, with quantitative assessment of immune cells, fibroblasts, and tertiary lymphoid structures using QuPath-based image analysis.

REFERENCES & ACKNOWLEDGEMENTS



DISCUSSION AND CONCLUSION

Actionable Take Away Message

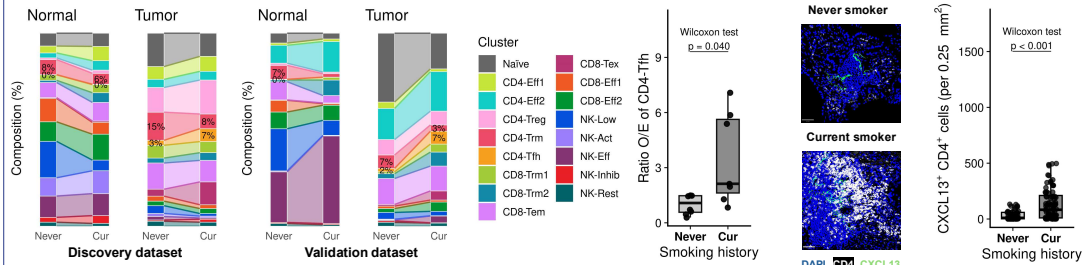
- Smoking-associated LUAD TME remodeling is characterized by enrichment of CXCL13⁺ CD4⁺ Tfh cells, B-cell accumulation, and increased TLS formation.
- The CXCL13⁺ Tfh-B-cell axis and VCAM1⁺FAP⁺ fibroblast-rich niches may serve as candidate biomarkers of TLS-related immune organization and help refine immunotherapy stratification.

Future Direction for Research

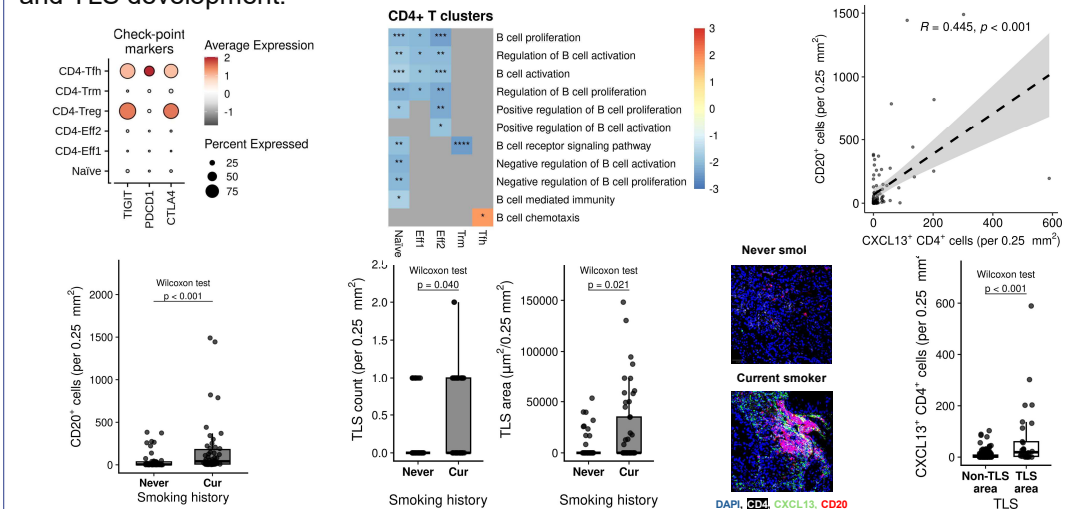
- Larger, multicenter ICI-treated cohorts are needed to determine whether CXCL13⁺ Tfh cells, TLS burden, and VCAM1⁺FAP⁺ fibroblasts predict treatment response and outcomes.
- Functional and spatial studies are needed to clarify how CXCL13⁺ Tfh cells, B cells, and VCAM1⁺ fibroblasts contribute to TLS formation and whether these pathways are therapeutically targetable.

RESULTS

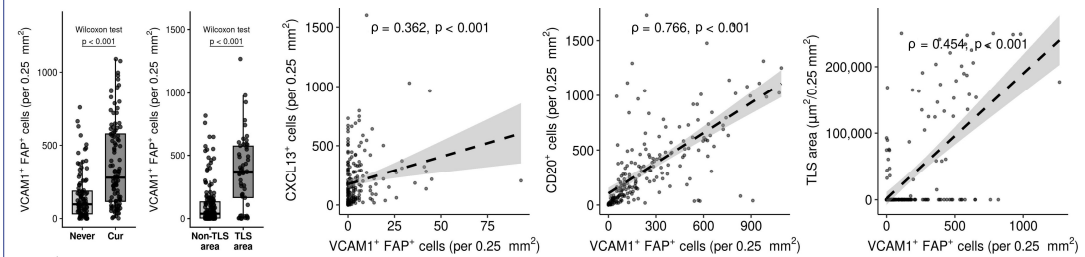
1. The CXCL13⁺ T follicular helper (Tfh) cells are enriched in TME of current smokers.



2. CD4⁺ Tfh cells exhibited high expression of multiple immune checkpoint molecules, and the expression of these genes within the TME was associated with B-cell accumulation and TLS development.



3. VCAM1⁺ fibroblasts were also more abundant in current smokers and were associated with the enrichment of CXCL13⁺ Tfh cells and B cells, as well as TLS development.



Artificial Intelligence (AI) Use Disclaimer

No AI tools were used in this presentation.