

# **Pan-cancer analysis of tumor microenvironments cell-cell interactions using large-scale scRNAseq and Visium data**

Jaewoo Mo<sup>1\*</sup>, Hoebin Chung<sup>1\*</sup>, Gahyun Kim<sup>1</sup>, Jeongbin Park<sup>2</sup>, Woong-Yang Park<sup>3,4,5,@</sup>, Junil Kim<sup>1,6@</sup>

*<sup>1</sup>Department of Bioinformatics, Soongsil University, 369 Sangdo-Ro, Dongjak-Gu, Seoul,*

*<sup>2</sup>Department of Information Convergence Engineering, Pusan National University, Yangsan,*

*<sup>3</sup>Department of Digital Health, Samsung Advanced Institute for Health Science and Technology, Sungkyunkwan University, Seoul, <sup>4</sup>Samsung Genome Institute, Samsung Medical Center, Seoul, <sup>5</sup>Department of Molecular Cell Biology, Sungkyunkwan University School of Medicine, Suwon, <sup>6</sup>School of Systems Biomedical Science, Soongsil University, 369 Sangdo-Ro, Dongjak-Gu, Seoul, Republic of Korea*

\* These authors contributed equally as co-first authors.

@To whom correspondence should be addressed to WYP (E-mail: woonyang.park@samsung.com) JK (Tel: +82-2-820-0452; E-mail: junilkim@ssu.ac.kr)

## **Grant Support**

This work was supported by the National Research Foundation of Korea (NRF) funded by the Korean Government (MSIT) [RS-2024-00342721, RS-2024-00440285, and RS-2023-00220207 to J.K.].

# Abstract

The tumor microenvironment (TME) is a complex network of tumor, immune, and non-immune stromal cells that collectively influence cancer progression and treatment response. Advances in single-cell RNA sequencing (scRNA-seq) allow detailed TME profiling, but spatial information is crucial for fully understanding cellular interactions in tumors. A pan-cancer analysis integrating scRNA-seq and spatial transcriptomics reveals cancer-type-specific diversity in cell type distributions and co-localization patterns. These differences underscore the unique micro-ecosystems of each cancer type, with distinctive co-localization patterns, especially between the immune and stromal cells. Analyzing relationships between cell type distribution and gene expression enables the identification of specific ligand-receptor pairs mediating interactions between epithelial and immune cells, illuminating immune regulatory mechanisms and spatially organized cellular interactions within tumors. These insights highlight the role of TME heterogeneity in immune dynamics and suggest pathways for targeted therapies tailored to the spatial and cellular complexity of each cancer type.