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Spatial arrangement of disease-associated molecular signatures in the neurodegenerative human brain at single-cell resolution

Se Young Jin, Baekgyu Choi, Jaeeun Park, Inkyung Jung*

Department of Biological Sciences, Korea Advanced Institute of Science and Technology (KAIST), Daejeon 34141, Republic of Korea

**Corresponding author : ijung@kaist.ac.kr*

Neurodegenerative diseases entail the progressive degeneration of diverse brain cells. Recent studies have identified the candidate pathogenic molecular signatures and investigated the cell type specific aberrant gene expression based on single-cell omics approaches. However, previous single cell omics approaches have been suffered from the lack of spatial information that may characterize intercellular mechanism and cell-to-cell interactions near the pathogen in the patient's brain. To overcome these limitations, we applied Multiplexed error-robust fluorescence in situ hybridization (MERFISH) to profile the spatial distribution of gene expression in single-cell resolution of the human brain tissue under neurotypical condition and Alzheimer's disease (AD) patients. Our spatial transcriptome results well capture disease specific gene expression patterns and reveal the combinatorial spatial distribution of disease-associated molecular signatures. Applying an imputation algorithm of spatial transcriptome, Tangram, further demonstrated the spatially clustered both known and novel disease-associated gene expression. Taken together, our results resolve the spatial distribution of disease associated molecular markers reflected pathological pathway in single-cell resolution.