Spatial and single-cell transcriptomics provide insights into the complex inflammatory cell network in atopic dermatitis

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RATIONALE: Atopic dermatitis (AD) is the most common chronic inflammatory skin disease with complex pathogenesis. SRecent studies including single-cell RNA-sequencing have demonstrated the complex inflammatory characteristics of AD skin. However, the detailed information on spatial and neighboring cells is still not fully understood.

METHODS: Skin tissues examined for spatial gene expression were derived from the upper arm of 6 healthy control (HC) donors and 7 AD patients (lesion and non-lesion). We performed Visium spatial transcriptomics sequencing. For single-cell analysis, we analyzed the single-cell data from suction blister material from the skin (4 ADs and 5 HCs) and full-thickness skin biopsies (4 ADs and 2 HCs). The multiple proximity extension assays were performed in the serum samples from 36 AD patients and 28 HCs.

RESULTS: The single-cell analysis identified unique clusters of fibroblasts, dendritic cells (DCs), and macrophages in the lesional AD skin. Spatial transcriptomics analysis showed the upregulation of COL6A5, TNC, CCL19 in COL18A1-expressing fibroblasts in the leukocyte-infiltrated areas in AD skin. CCR7-expressing DCs were also identified in the lesions. Additionally, M2 macrophages expressed CCL18 in the same localization. Ligand–receptor interaction analysis of the spatial transcriptome identified neighboring infiltration and interaction between activated TNC-expressing fibroblasts, CCL18-expressing M2 macrophages, LAMP3-expressing DCs, and T cells. As observed in skin lesions, serum levels of TNC and CCL18 were significantly elevated in AD and correlated with clinical disease severity.

CONCLUSIONS: In this study, we show the unknown cellular crosstalk in leukocyte-infiltrated area in lesional AD skin. Our findings provide an in-depth resource for the comprehensive characterization of AD.