Spatial transcriptomics and single-cell transcriptomics elucidates the intricate inflammatory cellular network in atopic dermatitis

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Atopic dermatitis (AD) is the most common chronic inflammatory skin disease. We aimed to investigate the complex spatial and neighboring inflammatory characteristics of AD skin. We performed Visium spatial transcriptomics sequencing in skin biopsies from 6 healthy control (HC) donors and 7 AD patients (lesion and non lesion). For single-cell analysis, we analyzed the previously published single-cell data from suction blister material and full-thickness skin biopsies (4 ADs and 5 HCs). The multiple proximity extension assays were performed in the serum samples from 36 AD patients and 28 HCs. 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*, *COL4A1*, *TNC*, and *CCL19* in COL18A1-expressing fibroblasts especially in the leukocyte-infiltrated areas in AD skin. Moreover, CCR7-expressing DCs and *CCL13*- and *CCL18-expressing* M2 macrophages showed a similar distribution in this lesion. Furthermore, ligand−receptor interaction analysis of the spatial transcriptome identified neighboring infiltration and interaction between activated COL18A1+ fibroblasts, *CCL18*+ M2 macrophages, *CCR7*+ 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. In this study, we demonstrate the characteristics of leukocyte-infiltrated areas in the upper dermis of AD skin as a tertiary lymphoid structures-like cellular infiltrate. These molecular interactions may play a central role in the lesion formation of AD.