Single-cell transcriptomic analysis highlights the significant role of inflammatory LYVE1+ macrophages in ovarian endometrioma

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Introduction/Background

Macrophages are a group of diverse and plastic immune cells which have critical roles in modulating immune responses, angiogenesis, and extracellular matrix remodelling. While macrophages are implicated in the pathogenesis of endometriosis, macrophage heterogeneity in human endometriosis remains poorly understood.

Materials and Methods

Single-cell suspensions of ectopic ovarian endometrioma tissues and the matched eutopic endometrial tissues were acquired from four patients with stage IV endometriosis based on the revised American Society of Reproductive Medicine score. CD45+ immune cells and CD45- non-immune cells were sorted out separately and then subjected to 10X single-cell RNAseq. The data was processed and analyzed by Seurat package in R. Macrophages were subclustered for in-depth investigation. Cellular interactions were predicted by CellChat package.

Results

We profiled 25143 $CD45^+$ immune cell transcriptomes (Ectopic n=14223, Eutopic n=10920) and 26109 $CD45^-$ non-immune cell transcriptomes (Ectopic n=12529, Eutopic n=13580). Unbiased subclustering of 1938 macrophages (Ectopic n=1058, Eutopic n=880) in our datasets identified five macrophage clusters. Two macrophage clusters associated with eutopic endometrium corresponded to the two major tissue-resident macrophage populations which can be discriminated by their expression of a hyaluronic acid receptor LYVE1. The three endometrioma-associated macrophage clusters also express LYVE1 at high levels. They are

also featured by their high expression of genes related to inflammatory responses (S100 genes, TREM1), angiogenesis (THBS1, VEGFA, HBEGF), and extracellular matrix remodelling (TIMP1). Cellular interaction analysis predicted that inflammatory LYVE1^{+} macrophages actively interact with vasculatures, thus promoting inflammation and angiogenesis in ovarian endometrioma.

Conclusion
Inflammatory LYVE1^{+} macrophages are a critical macrophage population regulating immune responses, extracellular matrix remodelling and angiogenesis in ovarian endometrioma. It represents a promising therapeutic target for future endometriosis treatment. Macrophage populations in eutopic endometrium corresponded to the two major tissue-resident macrophage populations which have been reported cross tissues.

Key words: Macrophage, LYVE1, inflammation