



Abstract 2002 Figure 3 Phagocytic macrophages in lupus nephritis are infrequent in diabetic and hypertensive kidney disease. Fig. 3 Phagocytic macrophages (red outlines) and a small subset of *LYVE1*⁺ macrophages in lupus nephritis are infrequent in kidney biopsies from patients with diabetes and hypertension. Intrarenal myeloid cells from 155 lupus nephritis and 45 chronic kidney disease patients were integrated.

populations of CD16⁺ and CD14⁺ monocytes, and residential *LYVE1*⁺ and *LYVE1*⁻ macrophages (figure 1).

Interestingly each infiltrating and residential cellular subset appeared to differentiate into these phagocytic macrophages in our trajectory analysis, suggesting that distinct cellular subsets converged on this common phagocytic state (figure 1). These phagocytic macrophages were infrequent in kidney biopsies collected from patients with non-autoimmune kidney disease from hypertension and diabetes (figure 3). Together, our findings suggest that phagocytic macrophages may play an important role in kidney remodeling and that these cells originated from distinct infiltrating and residential populations in response to kidney lesions found in lupus nephritis.

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TISSUE-RESIDENT, EXTRAVASCULAR MONOCYTIC LIKE CELL IS CRITICAL FOR INFLAMMATION IN THE SYNOVIUM PERLMAN, HARRIS

10.1136/lupus-2022-lupus21century.108

Background In recent years, our understanding of the mononuclear phagocyte system has expanded, highlighting previously unknown complexities in cell origin and function. However, to date few studies have examined a role for monocytes in tissues, with the majority of studies centered on circulating monocytes, or monocyte-derived macrophages. While transcriptional studies have exposed critical gene signatures for classical monocytes (CM) and non-classical monocytes (NCM) in the bone marrow and circulation, no such studies examined heterogeneity and function at the tissue level.

Methods We utilized functional genomic analysis of murine and human synovium including single cell-CITE and ATAC seq.

Results Here, we identify and characterize intravascular (i.v.) and extravascular (e.v.) synovial monocyte populations (Syn Ly6c⁻ cells) which are distinct in surface marker expression and transcriptional profile from circulating monocytes, dendritic cells and tissue macrophages, and are conserved in patients with rheumatoid arthritis. e.v. Syn Ly6c⁻ cells are independent of NR4A1 and CCR2, long-lived and embryonically derived while the i.v. Syn Ly6c⁻ cells are dependent on NR4A1, short lived and derived from circulating monocytes. e.v. Syn Ly6c⁻ cells undergo increased proliferation and reverse diapedesis dependent on LFA1 in response to arthrogenic stimuli and are required for the development of inflammatory arthritis.

Conclusions These findings uncover a new facet of mononuclear cell biology and are imperative to understanding tissue-resident myeloid cell function in the synovium.

Transcriptomics

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GENE EXPRESSION PROFILING OF KEY IMMUNE/INFLAMMATORY PATHWAYS REVEALS MOLECULAR ENDOTYPES OF SLE WITH CLINICAL IMPLICATIONS

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10.1136/lupus-2022-lupus21century.109