A94 MYELOID CELL SUBSETS DYNAMIC DURING PROGRESSION OF MOUSE COLLAGEN-INDUCED ARTHRITIS

J Presumey,^{1,2} C Jorgensen,^{1–3} G Courties,^{1,2} F Apparailly^{1–3} ¹Inserm, U 844, Montpellier, France; ²UFR de Médecine, Université Montpellier 1, Montpellier, France; ³Service Clinique d'Immuno-Rhumatologie, CHU Lapeyronie, Montpellier, France

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Background and objectives Circulating monocytes consist at least of two main subsets of immune cells arising from a common progenitor in the bone marrow that can give rise to macrophages and dendritic cells upon entry into tissues.¹ Consistent with the recent description of three subpopulations of monocytes, previous studies performed in rheumatoid arthritis (RA) do not allow to fully understand their respective functions since generally only the classical CD14 monocytes are considered.² Interestingly, their mouse homologues are well defined in experimental models of autoimmunity, and a splenic 'reservoir' of true monocytes able to migrate into injured tissues to regulate inflammation has also been recently described.³ Nevertheless, the three monocyte populations are not described in mouse models of arthritis. The present study aimed at fully characterising monocyte subsets and monocyte-derived cells during the development of collagen-induced arthritis (CIA) to unravel their respective role in the RA pathogenesis.

Materials and methods Using flow cytometric immunophenotyping, the authors have analysed the expression of several specific myeloid cell markers, CD11b, Ly6C, Ly6G, CD43, CD115, F4/80, CD11c, PDCA1, CMHII in the mouse CIA model. Frequencies of the various cell subpopulations have been assessed in the blood, spleen, draining lymph nodes and inflamed joints at different stages of the disease, and compared to naïve mouse samples.

Results In the circulation, the Ly6C^{low} monocyte frequency drops after the boost (D21), and is followed by a sequential raise of Ly6C^{int} and Ly6C^{high} monocytes at later time points of disease. A Ly6C^{high} monocytosis is observed in the spleen from D21. In inflamed joints, the number of neutrophils increased from ~30% up to ~60% compared with steady state and represent the main source for local tumour necrosis factor α (TNF α) production. Surprisingly, monocytes/macrophages are found in significant amount within steady state joints (~2%) and their number increased during CIA (~5% of total cells). Finally, the subpopulation of Ly6C^{low} monocytes/macrophages observed in steady state conditions does not fluctuate within CIA joints while the Ly6C^{int/high} monocytes/macrophages increase over-time and produce high levels of TNF α .

Conclusion Overall, this data show that all three monocyte subsets are not only present within blood and lymphoid organs as previously described, but also within joints, in both steady state and pathological conditions, and their frequencies within these tissues fluctuates in a dynamic manner.

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