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Cell Development, Differentiation, & Trafficking

Distinct functions of CXCR4, CCR2, and CX3CR1 direct dendritic cell precursors from the bone marrow to the lung

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First published: 1 February 2017
https://doi.org/10.1189/jlb.1A0616-285R

Abstract

Precursors of dendritic cells (pre - DCs) arise in the bone marrow (BM), egress to the blood, and finally migrate to peripheral tissue, where they differentiate to conventional dendritic cells (cDCs). Upon their activation, antigen - bearing cDCs migrate from peripheral tissue to regional lymph nodes (LNs) in a manner dependent on the chemokine receptor, CCR7. To maintain immune homeostasis, these departing cDCs must be replenished by new cDCs that develop from pre - DCs, but the molecular signals that direct pre - DC trafficking from the BM to the blood and peripheral tissues remain poorly understood. In the present study, we found that pre - DCs express the chemokine receptors CXCR4, CCR2, and CX3CR1, and that each of these receptors has a distinct role in pre - DC trafficking. Flow cytometric analysis of pre - DCs lacking CXCR4 revealed that this receptor is required for the retention of pre - DCs in the BM. Analyses of mice lacking CCR2 or CX3CR1, or both, revealed that they promote pre - DC migration to the lung at steady state. CCR2, but not CX3CR1, was required for pre - DC migration to the inflamed lung. Thus, these multiple chemokine receptors cooperate in a step - wise fashion to coordinate the trafficking of pre - DCs from the BM to the circulation and peripheral tissues.

Supporting Information

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