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Toll-like receptor ligands regulate the migratory pattern of leukocytes

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Introduction

Directed cell migration to the inflammation sites is induced by inflammatory chemokines. Cells from the periphery can respond to gradients of these chemokines through chemokine receptors. Previous studies have shown the regulation of certain chemokine receptors by pathogens on isolated subpopulations of leukocytes or cell lines. However, little is known about the regulation of TLRs on the complex migratory pattern of peripheral blood leukocytes and the mediators involved in this regulation.

Aim

In order to understand the influence of pathogens on the migratory pattern of cells, we analyzed by flow cytometry how Toll-like receptor ligands can regulate the expression of chemokine receptors (CCR2, CCR4, CCR5, CCR6, CXCR3 and CXCR4) on different leukocyte subpopulations using whole blood cultures.

Methods

The expression of chemokine receptors (CCR2, CCR4, CCR5, CCR6, CXCR3 and CXCR4) on monocytes, lymphocytes and granulocytes were analyzed by flow cytometry in 20h whole blood cultures with TLR ligands (LPS for TLR4, Pam3CSK4 for TLR2:1 and FSL1 for TLR2:6).

Results

After the stimulation with TLR ligands, the expression of CCR2 and CXCR4 on monocytes decreased whereas the expression of CCR4, CCR5 and CXCR3 on monocytes and CXCR3 on lymphocytes increased. Since peripheral blood cell cultures with TLR ligands induced the production of TNF-alpha and IL-10, we analyzed whether the observed chemokine receptor modulation was the result of the direct binding of TLR ligands or the produced pro- and anti-inflammatory mediators. TNF-alpha as well as IL-10 decreased CCR2 and CXCR4 expression but increased CCR4 expression on monocytes. Blocking IL-10 or TNF-alpha effect in the TLR ligand cultures with neutralizing antibodies, completely restored the chemokine receptor expression on leukocytes.

Conclusion

TNF-alpha and IL-10 mediate TLR-mechanisms that can regulate leukocyte migration and traffic, influencing the progression of an inflammatory process.

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