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Is Chemokine Receptor CCR9 Required for Synovitis in Rheumatoid Arthritis? Deficiency of CCR9 in a Murine Model of Antigen-Induced Arthritis

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ABSTRACT

Objectives: Monocytes/macrophages accumulate in the synovial membrane in rheumatoid arthritis and play a key role in disease pathogenesis, contributing to inflammation, cartilage destruction and bone erosion. Identification of molecules involved in monocyte/macrophage recruitment in inflammation is crucial for development of therapeutic interventions. Chemokine receptor CCR9 is up-regulated on these cells in peripheral blood and synovium of rheumatoid patients. This study investigated the course of antigen-induced arthritis in CCR9 deficient C57BL/6 mice in comparison to wild type animals to determine whether CCR9 is critical for disease severity and progression. Methods: Methylated bovine serum albumin was used for induction of uni-lateral arthritis by direct injection into the knee joints of preimmunized animals. Arthritis is confined to the injected joint allowing comparison with the normal opposing joint. Clinical severity of arthritis was assessed by measuring swelling in the arthritic joint in comparison to the normal joint. Histological analysis was performed to assess the extent of leukocyte infiltration and cartilage depletion. Results: Levels of swelling were not significantly different between wild type and CCR9 deficient mice. Similarly there was no significant difference in histological severity of arthritis when comparing CCR9-deficient mice to wild type mice. Conclusions: CCR9 was not required for development of synovial inflammation and cartilage destruction in the anti-gen-induced model of arthritis in C57BL/6 mice in this study. This may reflect a true lack of a pathogenic role of CCR9 on monocyte/macrophage function in vivo or it may reflect differences in the current antigen-induced arthritis model when compared to human RA.

KEYWORDS

Chemokine Receptor CCR9; Rheumatoid Arthritis; Inflammation; Antigen-Induced Arthritis; Mouse Mod-el; Monocytes/Macrophages

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