OJRA> Vol.2 No.4, November 2012

Open Access

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

PDF (Size:1131KB) Full-Text HTML, PP. 77-84 DOI: 10.4236/ojra.2012.24015

Author(s)

Alison Cartwright, Sophie King, Jim Middleton, Oksana Kehoe

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

Cite this paper

A. Cartwright, S. King, J. Middleton and O. Kehoe, "Is Chemokine Receptor CCR9 Required for Synovitis in Rheumatoid Arthritis? Deficiency of CCR9 in a Murine Model of Antigen-Induced Arthritis," *Open Journal of Rheumatology and Autoimmune Diseases*, Vol. 2 No. 4, 2012, pp. 77-84. doi: 10.4236/ojra.2012.24015.

References

[1] Y. Ma and R. M. Pope, "The Role of Macrophages in Rheumatoid Arthritis," Current Pharmaceutical Design, Vol. 11, No. 5, 2005, pp. 569-580. doi:10.2174/1381612053381927

[2] R. W. Kinne, B. Stuhlmüller and G. R. Burmester, "Cells of the Synovium in Rheumatoid Arthritis: Macrophages," Arthritis Research and Therapy, Vol. 9, 2007, p. 224. doi:10.1186/ar2333

[3] D. Mulherin, O. Fitzgerald and B. Bresnihan, "Synovial Tissue Macrophage Populations and Articular Damage in Rheumatoid Arthritis," Arthritis and Rheumatism, Vol. 39, No. 1, 1996, pp. 115-124. doi:10.1002/art.1780390116

[4] B. A. Zabel, W. W. Agace, J. J. Campbell, H. M. Heath, D. Parent, A. I. Roberts, E. C. Ebert, N. Kassam, S. Qin, M. Zovko, G. J. LaRosa, L. L. Yang, D. Soler, E. C. Butcher, P. D. Ponath, C. M. Parker and D. P. Andrew, "Human G Protein-Coupled Receptor GPR-9-6/CC Chemokine Receptor 9 Is Selectively Expressed on Intestinal homing T Lymphocytes, Mucosal Lymphocytes, and Thymocytes and Is

OJRA Subscription
Free Newsletter Subscription
Most popular papers in OJRA
Publication Ethics Statement
About OJRA News
Frequently Asked Questions
Recommend to Peers
Recommend to Library
Contact Us

Required for Thymus-Expressed Chemokine-Mediated Chemotaxis, Journal of Experimental Medicine, Vol. 190, No. 9, 1999, pp. 1

[5] E. J. Kunkel, J. J. Campbell, G. Haraldsen, J. Pan, J. Boisvert, A. I. Roberts, E. C. Ebert, M. A. Vierra, S. B. Goodman, M. C. Genovese, A. J. Wardlaw, H. B. Greenberg, C. M. Parker, E. C. Butcher, D. P. Andrew and W. W. Agace, "Lymphocyte CC Chemokine Receptor 9 and Epithelial Thymus-Expressed Chemokine (TECK) expression Distinguish the Small Intestinal Immune Compartment: Epithelial Expression of Tissue-Specific Chemokines as an Organizing Principle in Regional Immunity," Journal of Experimental Medicine

[6] Z. Qiuping, L. Qun, H. Chunsong, Z. Xiaolian, H. Baojun, Y. Mingzhen, L. Chengming, H. Jinshen, G. Qingping, Z. Kejian, S. Zhimin, Z. Xuejun, L. Junyan and T. Jinquan, "Selectively Increased Expression and Functions of Chemokine Receptor CCR9 on CD4+ T cells from Patients with T-Cell Lineage Acute Lymphocytic Leukaemia," Cancer Research, Vol. 63, No. 19, 2003, pp. 6469-6477.

[7] F. F. Amersi, A. M. Terando, Y. Goto, R. A. Scolyer, J. F. Thompson, A. N. Tran, M. B. Faries, D. L. Morton and D. S. Hoon, "Activation of CCR9/CCL25 in Cutaneous Melanoma Mediates Preferential Metastasis to the Small Intestine," Clinical Cancer Research, Vol. 14, 2008, pp. 638-645. doi:10.1158/1078-0432.CCR-07-2025

[8] S. Singh, U. P. Singh, J. K. Stiles, W. E. Grizzle and J. W. Lillard Jr., "Expression and Functional Role of CCR9 in Prostate Cancer Cell Migration and Invasion," Clinical Cancer Research, Vol. 18, No. 21, 2004, pp. 8743-8750. doi:10.1158/1078-0432.CCR-04-0266

[9] E. L. Johnson, R. Singh, S. Singh, C. M. Johnson-Holiday, W. E. Grizzle, E. E. Partridge and J. W. Lillard Jr., "CCL25-CCR9 Interaction Modulates Ovarian Cancer Cell Migration, Metalloproteinase Expression, and Invasion," World Journal of Surgical Oncology, Vol. 8, 2010, p. 62. doi:10.1186/1477-7819-8-62

[10] C. Johnson-Holiday, R. Singh, E. Johnson, S. Singh, C. R. Stockard, W. E. Grizzle and J. W. Lillard Jr., "CCL25 Mediates Migration, Invasion and Matrix Metalloproteinase Expression by Breast Cancer Cells in a CCR9-Dependent Fashion," International Journal of Oncology, Vol. 38, No. 5, 2011, pp. 1279-1285.

[11] B. Eksteen and D. H. Adams, "GSK-1605786, a Selective Small-Molecule Antagonist of the CCR9 Chemokine Receptor for the Treatment of Crohn's Disease," IDrugs, Vol. 13, No. 7, 2010, pp.472-781.

[12] M. J. Walters, Y. Wang, N. Lai, T. Baumgart, B. N. Zhao, D. J. Dairaghi, P. Bekker, L. S. Ertl, M. E. Penfold, J. C. Jaen, S. Keshav, E. Wendt, A. Pennell, S. Ungashe, Z. Wei, J. J. Wright and T. J. Schall, "Characterization of CCX282-B, an Orally Bioavailable Antagonist of the CCR9 Chemokine Receptor, for Treatment of Inflammatory Bowel Disease," Journal of Pharmacology and Ex- perimental Therapeutics, Vol. 335, No. 1, 2010, pp. 61-69. doi:10.1124/jpet.110.169714

[13] C. Schmutz, A. Cartwright, H. Williams, O. Haworth, J. H. Williams, A. Filer, M. Salmon, C. D. Buckley and J. Middleton, "Monocytes/Macrophages Express CCR9 in Rheumatoid Arthritis and CCL25 Stimulates Their Differentiation," Arthritis Research and Therapy, Vol. 12, No. 4, 2010, pp. R161. doi:10.1186/ar3120

[14] D. Brackertz, G. F. Mitchell and I. R. Mackay, "Anti- gen-Induced Arthritis in Mice," Arthritis and Rheumatism, Vol. 20, No. 3, 1977, pp. 841-850. doi:10.1002/art.1780200314

[15] W. B. van den Berg, L. A. Joosten and P. L. van Lent, "Murine Antigen-Induced Arthritis," Methods in Mole- cular Medicine, Vol. 136, No. 2, 2007, pp.243-253. doi:10.1007/978-1-59745-402-5_18

[16] M. A. Nowell, P. J. Richards, S. Horiuchi, N. Yamamoto, S. Rose-John, N. Topley, A. S. Williams and S. A. Jones, "Soluble IL-6 Receptor Governs IL-6 Activity in Expe- rimental Arthritis: Blockade of Arthritis Severity by Soluble Glycoprotein," Journal of Immunology, Vol. 171, 2003, pp. 3202-3209.

[17] A. Mantovani, A. Sica and M. Locati, "New Vistas on Macrophage Differentiation and Activation," European Journal of Immunology, Vol. 37, No. 1, 2007, pp.14-16. doi:10.1002/eji.200636910

[18] M. Corr and B. Crain, "The Role of FcgammaR Signaling in the K/B × N Serum Transfer Model of Arthritis," Journal of Immunology, Vol. 169, No. 11, 2002, pp. 6604-6609.

[19] J. P. Jacobs, A. Ortiz-Lopez, J. J. Campbell, C. J. Gerard, D. Mathis and C. Benoist, "Deficiency of CXCR2, but Not Other Chemokine Receptors, Attenuates a Murine Model of Autoantibody-Mediated Arthritis," Arthritis and Rheumatism, Vol. 62, No. 7, 2010, pp.1921-1932.

[20] N. Nakamoto, H. Ebinuma H, T. Kanai, P. S. Chu, Y. Ono, Y. Mikami, K. Ojiro, M. Lipp, P. E. Love, H. Saito and T. Hibi, "CCR9(+) Macrophages Are Required for Acute Liver Inflammation in Mouse Models of Hepatitis," Gastroenterology, Vol. 142, No. 2, 2012, pp.366-376. doi:10.1053/j.gastro.2011.10.039

[21] B. Johansson-Lindbom and W. W. Agace, "Generation of Gut-Homing T Cells and Their Localization