there is a lack of relevant reports on their function in chronic, multisystem autoimmune diseases.

Objectives: Here, using molecular biology techniques were performed to evaluate the expression of 7 chemokines/chemokine receptors in different tissues and their localization in the joints.

Methods: We established a collagen-induced arthritis (CIA) model in female Wistar rats and evaluated the expression patterns of 7 chemokines/chemokine receptors (CCR3, CCR5, CCR7, CCL5, CXCR3, CXCR4, and CXCL10) in different tissues using qRT-PCR and western blotting and their localization in the joints using immunohistochemistry.

Results: The mRNA expression of *CCR3*, *CCR7*, *CXCR4*, and *CXCL10* was significantly higher in the spleen and joints, while that of *CCR5* and *CCL5* was significantly higher in the liver and that of *CXCR3* was significantly higher in the lung, spleen, and joints (Fig. 1). Protein expression patterns largely corresponded to mRNA expression patterns. In the joints, CCR3, CCR5, and CCR7 were expressed in fibroblast-like synoviocytes (FLS), macrophages, stromal cells, and endothelial cells. CCL5, CXCR3, and CXCR4 were expressed in FLS, endothelial cells, and stromal cells. CXCL10 was expressed throughout the synovium, stromal cells, and endothelial cells (Fig. 2).

Figure 1. Relative expression levels of seven chemokine/chemokine receptor genes in different tissues of CIA rats

Figure 2. Representative images of immunostaining of chemokines and their receptors in CIA rat joints. Arrow, FLS; triangle, endothelial cell; pentagon, stromal cell; chevron, macrophage. A–G. Positive immunohistochemistry results for CCR3, CCR5, CCR7, CCL5, CXCR3, CXCR4, and CXCL10, respectively; H. Negative control. Scale bar, 200 μ m.

Conclusion: Seven chemokines/chemokine receptors are widely expressed in different tissues in the CIA rat model, and all are involved in the inflammatory response. Our results provide a basis for investigations into the mechanism of action of RA and suggest that chemokines may become novel targets for RA treatment.

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TNF INHIBITION IN RHEUMATOID ARTHRITIS RESPONDERS TO CERTOLIZUMAB-PEGOL REDUCES LYMPHOCYTE RECRUITMENT FROM BLOOD WHILE MONOCYTE TURNOVER REMAINS INCREASED

Biljana Smiljanovic¹, Till Sörensen², Marc Bonin², Pascal Schendel², Sascha Johannes², Karl Skriner², Marina Backhaus³, Silvia Pade², Gabriela Schmittat², Sandra Hermann², Sarah Ohrndorf², Bruno Stuhlmlüller², Andreas Grützkau⁴, Gerd Rüdiger Burmester², Thomas Häupl². ¹Charité – Universitätsmedizin Berlin, Rheumatology, Berlin, Germany; ²Charité – Universitätsmedizin Berlin, Rheumatology, Berlin, Germany; ³Park-Klinik Weißensee, Berlin, Germany; ⁴Deutsches Rheuma-Forschungszentrum (DRFZ), Berlin, Germany

Background: Increased turnover of monocytes is a hallmark of active RA¹. Targeting the mediators of monocyte activation like TNF or IL6 is a successful strategy in reducing inflammation in RA.

Objectives: To investigate differential effects of anti-TNF treatment in responders and non-responder on turnover of peripheral leukocytes in patients with rheumatoid arthritis.

Methods: Immune cell profiling in a subgroup of 36 patients of the BIORAC open-label 52-weeks treatment study with certolizumab-pegol (CZP) by multicolor flow cytometry at baseline, week 12 and 52. Cell populations were analyzed with *immunoClust*²

Results: Of the 36 RA patients with initial DAS28 of 4.75, response to CZP occurred in 18 patients after 12 weeks and 15 patients after 52 weeks (both Δ -DAS28 -1.4). When comparing populations during the course of treatment, there was no relevant change in the number of monocytes or granulocytes. However, as previously reported¹, the most characteristic observation was the reduced absolute number of non-classical CD16⁺CD14^{low} monocytes at baseline when compared to healthy controls. This corresponds to increased monocyte turnover and recruitment to inflamed tissue. In both, responders and non-responders this monocyte population did not increase or change over time despite reduction of DAS28 disease activity in responders. In responders to CZP, the absolute number of T-cells, B-cells and NK-cells as well as their subsets including naïve-, central- and effector-memory T-cells and naïve-, unswitched- and switched memory B-cells and plasmablasts increased compared to baseline. In non-responders to CZP, the absolute number of T-cells, B-cells and NK-cell remained unchanged. In CZP responders, the cell frequencies in T-cell subsets shifted from a naïve towards a central and effector phenotype, while in non-responder no changes were identified.

Conclusion: In responders, successful reduction of subsequent events of immune activation by anti-TNF drugs will decrease inflammation and thus decrease recruitment of lymphocytes to tissue. Initial triggering seems to involve especially monocytes, which are typical producers of TNF and which are still recruited to tissue much more than in healthy controls as indicated by persisting reduction of non-classical monocytes even in responders. Thus, increase of lymphocytes in the blood upon response seems to reflect ongoing mobilization from bone marrow and lymphatic organs into the blood but reduced recruitment to tissues when local inflammation is successfully suppressed. Altogether, these changes indicate that triggers for monocyte recruitment exist and persist despite immunosuppression with anti-TNF whereas lymphocyte recruitment is successfully suppressed in responders to anti-TNF.

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